DOCUMENT RESUME

ED 254 813 CG 018 100

TITLE	Alcohol and Health. Fifth Special Report to the U.S. Congress from the Secretary of Health and Human Services.
INSTITUTION	National Inst. on Alcohol Abuse and Alcoholism (DHHS), Rockville, Md.
REPORT NO	DHHS-(ADM)-84-1291
PUB DATE	Dec 83
NOTE	170p.
AVAILABLE FROM	Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.
PUB TYPE	Information Analyses (070)
EDRS PRICE	MF01/PC07 Plus Postage.
DESCRIPTORS	*Alcoholism; Drinking; Etiology; Health; Heredity; *Physical Health; Pregnancy; *Prevention; Social Problems; Traffic Accidents

ABSTRACT

This report is divided into an overview of alcohol and health, and eight chapters which deal with various aspects of alcohol use and abuse. The epidemiology of alcohol abuse and alcoholism is discussed. Data are presented on self-reported consumption of alcohol among youths and adults; alcohol consumption during pregnancy; alcohol-related hospitalizations and mortality; alcohol problems in veterans and native Americans; and alcohol-related traffic fatalities. Early and recent studies on the heritability of alcoholism are reviewed, the environmental-genetic influences on alcoholism are considered, and human and animal studies on the genetic factors in physiological responses to alcohol are explained. In a discussion of psychobiological effects of alcohol, cognitive and neurophysiological effects, neuropathologic illnesses, electrophysiology, and neural and biochemical effects are considered, and theories of the effects of alcohol are reviewed. The medical consequences of alcohol are discussed in terms of alcohol and the digestive system, the liver, muscle systems, blood disorders, kidney disease, pulmonary disease, the endocrine system, and alcohol and cancer. The effects of alcohol on pregnancy outcome are discussed. Adverse social consequences of alcohol use and abuse are described, including alcohol-related accidents, crime, domestic problems, and suicide. Treatment trends in research and practice are discussed and preventive efforts are reviewed. (NRB)

****
* Reproductions supplied by EDRS are the best that can be made *
* from the original document. *
****

ED254813

FIFTH SPECIAL REPORT TO THE U.S. CONGRESS ON

ALCOHOL AND HEALTH

FROM THE SECRETARY OF HEALTH AND HUMAN SERVICES

DECEMBER 1983

U.S. DEPARTMENT OF EDUCATION
NATIONAL INSTITUTE OF EDUCATION
EDUCATIONAL RESOURCES INFORMATION CENTER (ERIC)

X This document has been reproduced as received from the person or organization originating it.
Minor changes have been made to improve reproduction quality.

• Points of view or opinions stated in this document do not necessarily represent official NIE position or policy.

CG 018100

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

National Institute on Alcohol Abuse and Alcoholism
5600 Fishers Lane
Rockville, Maryland 20857

This publication may be reproduced in any quantity desired. It is in the public domain and no permission is required. Citation of the source is appreciated. (NIAAA)

DHHS Publication No. (ADM) 84-1291
Printed 1984

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402

Contents

	Page
Foreword	v
Preface	vi
Acknowledgments	vii
Contributors	vii
Reviewers	viii
Introduction	x
Alcohol and Health -- An Overview	xiii
Defining Alcoholism and Heavy Drinking	xiii
Alcoholism and Heredity	xiii
Alcohol and the Brain	xv
Other Health Hazards	xvi
Adverse Social Consequences	xviii
Treatment Trends	xx
Prevention	xxii
Future Directions	xxiii
Chapter I. Epidemiology of Alcohol Abuse and Alcoholism	1
Consumption of Alcoholic Beverages Measured by Alcohol Sales	1
Surveys of Self-Reported Consumption Among Adults	2
Surveys of Alcohol Consumption Among Youth and Young Adults	3
Surveys of Alcohol Consumption During Pregnancy	5
Alcohol-Related Mortality Attributed to Alcoholism, Alcoholic Psychosis, and Liver Cirrhosis	6
Alcohol-Related Causes of Hospitalization	7
Alcohol-Related Problems in Veterans	8
Alcohol-Related Problems Among Native Americans	8
Alcohol-Related Motor Vehicle Fatalities	9
Summary	11
References	13
Chapter II. Genetics and Alcoholism	15
Heritability of Alcoholism--Early Studies	15
Heritability of Alcoholism--Recent Studies	16
Environmental-Genetic Influence on Alcoholism	17
Genetic Factors in Physiological Responses to Alcohol	19
Potential Mechanisms of Genetic Influence	21
Summary	22
References	22
Chapter III. Psychobiological Effects of Alcohol	25
Cognitive and Neurophysiological Effects	25
Neuropathologic Illnesses	28
Electrophysiology	30
Neural and Biochemical Effects	31

Theories of Alcohol's Effects 37
Summary 39
References 39

Chapter IV. Medical Consequences of Alcohol 45
Alcohol and the Digestive System 45
Alcohol and the Liver 48
Alcohol and Muscle Systems 51
Alcohol and Blood Disorders 53
Alcohol and Kidney Disease 54
Alcohol and Pulmonary Disease 54
Alcohol and the Endocrine System 55
Alcohol and Cancer 59
Summary 59
References 60

Chapter V. The Effects of Alcohol on Pregnancy Outcome 69
Historical Perspective 69
Fetal Alcohol Syndrome and Alcohol-Related Birth Effects 70
Prevalence 70
Problems with Human Fetal Alcohol Studies 71
Animal Models 71
Specific Adverse Pregnancy Outcomes 72
Alcohol Use, Abuse, and Dependence and Pregnancy 75
Implications of Current Knowledge--Frontiers 77
Summary 78
References 79

Chapter VI. Adverse Social Consequences of Alcohol Use and Alcoholism 83
Alcohol and Accidents 83
Alcohol and Crime 87
Alcohol and the Family 89
Alcohol and Suicide 92
Economic Costs of Alcohol Abuse 93
Summary 95
References 96

Chapter VII. Treatment: Emerging Trends in Research and Practice 100
Recent Advances in Diagnosis and Nomenclature 100
Screening and Early Detection of Alcoholism 104
Alcoholism Treatment: Programs and Therapeutic Approaches 105
Therapeutic Approaches 109
Factors Affecting Treatment Outcome 113
Emerging Trends and Future Directions 115
Summary 116
References 117

Chapter VIII. Prevention: A Broad Perspective 122
Current Perspectives 122
Education, Information, and Training 123
Law and Regulation 130
Current Activities 133
Summary 136
References 137

Index 142

Foreword

As this report so amply documents, the price of alcohol abuse to the American people is appallingly high. And that price is paid by all of us. The cost to our economy has been estimated at over $49 billion each year. But the dollar cost is only the beginning. The cost in human pain and misery, disease, and death is still more staggering. Accidents on our streets and highways claim about 50,000 Americans' lives each year--leaving another 150,000 permanently disabled. Half of those tragedies are alcohol related. Alcohol's role in disrupting family life is less easily documented, but few doubt that it is significant. One in three Americans surveyed last year felt that alcohol caused problems in his or her family.

Fortunately, this long-neglected problem has now become of increasing concern to many Americans. As a result of citizen action, drunk driving, once largely ignored, is now being taken seriously. More and more States are enacting tougher laws to discourage driving after drinking. Treating alcoholics once was of interest to a few dedicated men and women--themselves often recovering alcoholics. Treatment now involves many thousands in the helping professions as well. In industry, many, perhaps most, companies are coming to recognize that losing a valued employee to alcoholism is costly--and that making provision for treatment just makes good business sense. Many health insurance plans are providing benefits to treat alcoholism itself as they discover it costs much less in the long run than treating its chronic health consequences.

Perhaps the most encouraging sign is the increasing awareness Americans are developing that we ourselves have a primary responsibility for preserving our well-being by practicing better health habits--including moderation in alcohol consumption.

This report deserves to be widely read--and its implications thoughtfully considered. Through our combined efforts, we can sharply reduce alcohol abuse and its devastating consequences.

Margaret M. Heckler
Secretary of Health and Human Services
December 1983

Preface

This has been a century of impressive achievement in public health. The advent of vaccines against such diseases as smallpox, diphtheria, and polio and their widespread application have virtually eliminated those once dreaded illnesses. Tuberculosis, the cause of one in eight deaths in 1900, is now uncommon and still more rarely fatal. Antibiotics have made most infectious diseases easily curable. But the devastation of one disease has not yet been significantly eroded. It plays a role in 10 percent of all deaths in the United States. In some segments of the population, it produces still higher mortality. It is the principal cause of deaths through accidents among those aged 15 to 24. That malady is, of course, alcohol abuse.

Alcohol abuse during pregnancy has been found to cause fetal alcohol syndrome and other alcohol-related birth defects. Fetal alcohol syndrome appears to be one of the leading known teratogenic causes of mental retardation. There is reason to believe that alcohol may be injurious to the developing fetus at dose levels no higher than those often consumed by those who drink moderately.

In adults, alcohol abuse is the leading cause of liver cirrhosis (the eighth leading cause in the United States), the leading contributing factor for chronic pancreatitis, and has been implicated in a wide range of other illnesses as well.

As this and previous Alcohol and Health reports indicate, the increased Federal role in this area has markedly altered an earlier pessimistic outlook with respect to treating those dependent on alcohol. We no longer believe that the alcoholic must reach the late stages of the illness before he or she can benefit from help. On the contrary, as in other illnesses, there is good evidence that the earlier treatment begins, the greater is the likelihood of successful recovery.

Alcohol research has provided us with greater insight into the underlying mechanisms of alcohol dependence. It is by no means visionary to say that our enhanced understanding holds the promise not only of improved treatment, but of preventing alcohol dependence before it develops. We may not be far from the day when simple laboratory tests can determine those who are at greatest risk of becoming alcoholic--before they take that first drink.

The Fifth Special Report, together with its predecessors, provides valuable insight into the impressive progress that has been made--and the distance yet to be traveled before we resolve this major public health problem.

Edward N. Brandt, Jr., M.D.
Assistant Secretary for Health

Acknowledgments

This Fifth Special Report on Alcohol and Health is the product of many people's efforts in reviewing and summarizing hundreds of scientific papers, begun shortly after the Fourth Special Report was forwarded to the U.S. Congress in 1981. The chief contributors, many of whom also contributed to previous reports, include some of the most distinguished scientists and knowledgeable alcoholism researchers and medical authorities in the world today.

Equally important roles were played by individuals who provided professional review of the preliminary report. The combined efforts are reflected in every chapter of the report.

Contributors

Harold L. Altshuler, Ph.D.
Texas Research Institute of Mental Sciences
Texas Medical Center
Houston, Texas

Thomas F. Babor, Ph.D., M.P.H.
Department of Psychiatry
University of Connecticut
School of Medicine
Farmington, Connecticut

Herbert Barry III, Ph.D.
Department of Pharmacology and Toxicology
University of Pittsburgh
Pittsburgh, Pennsylvania

Ralph Hingson, Sc.D.
School of Medicine
Boston University
Boston, Massachusetts

Paula L. Hoffman, Ph.D.
Department of Physiology and Biophysics
University of Illinois at the Medical Center
Chicago, Illinois

Ronald Kadden, Ph.D.
Department of Psychiatry
University of Connecticut
School of Medicine
Farmington, Connecticut

Charles Kaelber, M.D.
Division of Biometry and Epidemiology
National Institute on Alcohol Abuse
and Alcoholism
Rockville, Maryland

Ting-Kai Li, M.D.
Indiana University
School of Medicine
Indianapolis, Indiana

Henry Malin
Acting Chief
Surveillance Branch
Division of Biometry and Epidemiology
National Institute on Alcohol Abuse
and Alcoholism
Rockville, Maryland

Peter R. Martin, M.D.
Acting Chief
Section of Clinical Science
Laboratory of Clinical Studies
National Institute on Alcohol Abuse
and Alcoholism
Rockville, Maryland

Barbara S. McCrady, Ph.D.
Center of Alcohol Studies
Rutgers University
Piscataway, New Jersey

Roger E. Meyer, M.D.
Department of Psychiatry
University of Connecticut
School of Medicine
Farmington, Connecticut

Peter E. Nathan, Ph.D.
Alcohol Behavior Research Laboratory
Rutgers University
New Brunswick, New Jersey

Robert J. Sokol, M.D.
Wayne State University
Department of Obstetrics and Gynecology
Detroit, Michigan

Boris Tabakoff, Ph.D.
Department of Physiology and Biophysics
University of Illinois at the Medical Center
Chicago, Illinois

David H. Van Thiel, M.D.
University of Pittsburgh
School of Medicine
Pittsburgh, Pennsylvania

Diana Walsh, Ph.D.
School of Medicine
Boston University
Boston, Massachusetts

Reviewers

James Beard, Ph.D.
University of Tennessee
College of Medicine
Memphis, Tennessee

Linda J. Beckman, Ph.D.
University of California at Los Angeles
Department of Psychiatry
Los Angeles, California

Henri Begleiter, Ph.D.
Department of Psychiatry
SUNY Downstate Medical Center
Brooklyn, New York

Nancy L. Day, Ph.D.
Department of Psychiatry and Epidemiology
Western Psychiatric Institute and Clinic
University of Pittsburgh
Pittsburgh, Pennsylvania

Richard A. Deitrich, Ph.D.
University of Colorado
Health Sciences Center
Denver, Colorado

Ivan Diamond, M.D., Ph.D.
University of California
School of Medicine
San Francisco, California

Herman Diesenhaus, Ph.D.
Colorado State Department of Health
Denver, Colorado

Terryl T. Foch, Ph.D.
Pennsylvania State University
College of Human Development
University Park, Pennsylvania

Donald W. Goodwin, M.D.
University of Kansas
School of Medicine
Kansas City, Kansas

Richard Jessor, Ph.D.
University of Colorado
Institute of Behavioral Sciences
Boulder, Colorado

Benjamin Kissin, M.D.
State University of New York
College of Medicine
Department of Psychiatry
Brooklyn, New York

Gerald E. McCleam, Ph.D.
Pennsylvania State University
College of Human Development
University Park, Pennsylvania

William C. McCready, Ph.D.
National Opinion Research Center
University of Chicago
Chicago, Illinois

Marlene Oscar-Berman, Ph.D.
School of Medicine
Boston University
Boston, Massachusetts

Carrie Randall, Ph.D.
Medical University of South Carolina
Charleston, South Carolina

Theodore Reich, M.D.
Psychiatrist-in-Chief
Jewish Hospital
St. Louis, Missouri

Robin Room, Ph.D.
Pacific Medical Center
San Francisco, California

Steven Schenker, M.D.
University of Texas
Health Science Center
San Antonio, Texas

Brian Suarez, Ph.D.
Washington University
Jewish Hospital
St. Louis, Missouri

Don Walker, Ph.D.
University of Florida
College of Medicine
Gainesville, Florida

James R. West, Ph.D.
University of Iowa
Iowa City, Iowa

Sharon Wilsnack, Ph.D.
University of North Dakota
School of Medicine
Grand Forks, North Dakota

A significant number of NIAAA staff members made major contributions to this report as technical reviewers and consultants. These individuals included Loran Archer, Deputy Director, NIAAA; Lois Chatham, Ph.D., Kenneth Warren, Ph.D., Helen Chao, Ph.D., Tina Vanderveen, Ph.D., Mark Green, Ph.D., Albert Pawlowski, Ph.D., Daniel Lettieri, Ph.D., Nathan Rosenberg, Ph.D., Norman Chang, Ph.D., and Elsie Taylor, Division of Extramural Research; Henry Malin, Division of Biometry and Epidemiology; William Gregory, Rita Albery, and Judi Funkhouser, Division of Prevention and Research Dissemination; Susan Farrell and Joan White, Office of Policy Analysis; and Brenda Hewitt, Special Assistant to the Director, NIAAA.

Other individuals who made significant contributions were Robert Petersen, Ph.D., who served as a writer and provided technical assistance, particularly in the overview and other front matter, and Samuel Rosenfeld, a science writer who participated during the early draft stages of the report.

Introduction

To know where you are, it is often useful to look back at where you've been. Less than 15 years ago, a major U.S. Government publication described the problem of alcohol abuse in America as follows:

> No other national health problem has been so seriously neglected as alcoholism. Many doctors decline to accept alcoholics as patients. Most hospitals refuse to admit alcoholics. Available methods of treatment have not been widely applied. Research on alcoholism and excessive drinking has received virtually no significant support.[1]

It went on to laud the transition from an "atmosphere of moral disapproval" in which alcoholics were treated as "sinners or criminals" to the recognition that alcoholism is an illness. Only 3 years before, a U.S. Court of Appeals, in a precedent-setting decision, held that a homeless alcoholic's public drunkenness was involuntary. Up until then, nearly half of all arrests (excluding traffic offenses) were related to drunkenness. By 1968, Congress enacted the Alcoholic Rehabilitation Act (P.L. 90-574), declaring that "alcoholism is a major health and social problem" and that "the handling of chronic alcoholics within the system of criminal justice perpetuates and aggravates the broad problem of alcoholism whereas treating it as a health problem permits early detection and prevention . . . and effective treatment and rehabilitation. . . ."

This Act and subsequent legislation (P.L. 91-616) establishing the National Institute on Alcohol Abuse and Alcoholism (NIAAA) translated the long-held position of knowledgeable professionals that alcoholism was a treatable disease into national public policy. It officially declared, "Our task is not to punish, but to heal."

It is ironic that it took so long for public policy to reflect an informed consensus. Nearly 200 years ago, one of our country's most distinguished physicians, Dr. Benjamin Rush, labeled alcohol abuse an "addiction and a disease."[2] He also provided the first epidemiological estimate of the number of deaths each year from alcohol abuse. His estimate of 4,000 deaths annually in a population of 6 million (66.7 per 100,000) is surprisingly close to present estimates (as high as 93.2 per 100,000).

While the problems associated with alcohol are still very much with us, we at the Institute take satisfaction in what has been achieved in the 12 years since NIAAA was established. The first edition of the Alcohol and Health reports (1971) referred to alcoholism as an "iceberg problem," because social pressures caused so many with the disease to deny it. In the years since, the hidden portion of that iceberg has become more and more exposed. There have been important shifts in our attitudes toward drinking. Removing the moral onus from alcoholism made it easier for alcoholics to admit to having a disease rather than a defect of will. Organizations that previously stressed anonymity in their rehabilitation efforts have become more sympathetic to individual self-disclosure. Many of our leading citizens are now willing to "come out"--to acknowledge their own hard-fought battles with alcohol addiction. Their courage has made it easier for others to recognize that they too have alcohol problems--and to do so at an earlier stage.

There have been other benefits of more honestly recognizing that problems from alcohol abuse can occur at all levels of drinking and of the society. The still prevalent myth that drinking is "sophisticated," a necessary part of the "successful" life, is slowly being eroded. It now requires less social courage to refuse a drink or to request a nonalcohol substitute. The belief that drinking is essential to masculinity has been very much a part of

---

[1] U.S. Department of Health, Education, and Welfare. Alcohol and Alcoholism. National Clearinghouse for Mental Health Information Pub. No. 5011. Washington, D.C.: U.S. Government Printing Office, 1969.

[2] Rush, B. An Inquiry into the Effects of Ardent Spirits upon the Human Body and Mind; With an Account of the Remedies for Curing Them. (1785) Brookfield, Merriam, 8th ed. 1814.

American folklore. It is being supplanted by an increasing recognition of the health hazards of alcohol abuse and a new commitment to affirmation of good health practices. A public health revolution is underway with official recognition that the individual can do more for his or her own health than any doctor, hospital, drug, or other medical innovation. The past decade has clearly shown that habits as basic to personal health as smoking, diet, and exercise can be changed--and in a remarkably short time. Our success in changing behaviors that were once thought immutable provides good reason for optimism about alcohol abuse. As has become true of smoking, not drinking or drinking more moderately may become the "in" thing.

The carnage on our highways documented here and in earlier reports has also led to a new public appreciation of the gravity of mixing drinking with driving. Citizen groups have been impressively effective in changing public attitudes toward drinking and driving, making individuals more aware of just how much alcohol impairs driving skill.

Primary prevention--before drinking has even begun--may be one key to sharply reducing the high casualty rate from alcohol described in this report. Early intervention, between the sixth and ninth grades, is one means of educationally "inoculating" children against alcohol (and tobacco) abuse. Such efforts to teach good health habits early need to be carefully evaluated. As indicated here, most alcohol education efforts at older ages have been more successful in increasing knowledge about the drug, possibly altering expressed attitudes, but not in changing actual drinking.

Drinking during pregnancy is now known to pose risks for the health of the newborn. Programs directed toward women who have alcohol problems could sharply reduce the number of newborn who suffer such serious consequences of maternal drinking as the fetal alcohol syndrome and other alcohol-linked birth anomalies.

Treatment of alcoholism has come of age. Once largely confined to dedicated members of groups like Alcoholics Anonymous and a few committed professionals, treatment efforts in recent years have grown almost exponentially. Treating alcoholics is now "respectable"--and training for physicians and others to treat the alcohol-dependent person reflects this new found status.

There is an increased willingness to subject therapeutic efforts to research scrutiny--to determine what works best with whom and under what circumstances. Innovative employee assistance programs are now challenging the traditional belief that treatment must be completely voluntary to be successful. There is evidence that job-based referrals to treatment, provided early and in lieu of disciplinary action on the job, can be as effective as treatment sought on one's own. Treating alcohol dependence early is far more likely to succeed and is less costly to treat than intervention when this insidious disease is far advanced.

The fact that treating alcoholism within the framework of health insurance plans is cost-effective has now been proven repeatedly. There is no question that this leads to lower long-term health costs to the individual and the plan. Encouraging expansion of health insurance coverage to include adequate treatment of alcohol dependence is an important and continuing priority of the Institute.

The high costs of medical care are coming under more careful scrutiny. While a hospital was once thought to be the only suitable setting for detoxifying alcoholics, other settings may be equally effective--and much more cost-effective. Alternative treatment models employing certified alcoholism counselors have had demonstrated success. As the capabilities of these less expensive alternatives become apparent, health insurance programs should include them within their benefit structure.

A lack of agreement as to just what is meant by such terms as "alcohol abuse" and "alcoholism" has plagued us for many years. Because of it, comparing research and treatment outcomes has sometimes been difficult. We now recognize that alcohol abuse and alcoholism are both multidimensional with multiple causes. The newer modes of classification described in this report attempt to take this complexity into consideration.

One of the most satisfying developments in recent years has been research innovation. Federal support for alcohol research, once almost nonexistent, has had significant impact. By its very nature, basic research is a long-range enterprise, and its practical implications are often not immediately apparent. But studies of the ways in which alcohol alters the cellular anatomy and neurophysiology of the brain are already enlarging our understanding in ways that have practical "payoffs." A sensitive measure of the brain's electrical responses to sound and light stimulation may prove useful in determining those at greater

risk of becoming alcohol dependent. Other indications of the effects of alcohol on chemicals that govern nerve transmission are providing better explanations of just why certain symptoms of alcohol abuse occur. New neurophysiological explanations of how alcohol and other dependency-producing drugs operate offer the tantalizing possibility of some form of chemotherapy to reduce or even eliminate the likelihood of becoming alcohol dependent. While this is not a promise for the immediate future, it is an example of the kind of payoff that is unpredictable in the initial stages of basic research.

Biological markers described here--tests that distinguish heavy drinkers from others by measuring effects on the blood or other biological variables--are becoming valuable in the early diagnosis of those with drinking problems. Used in many kinds of settings, such tests can serve to alert the individual to the reality that he or she has an alcohol problem. There is now evidence that making patients aware of the results of such tests, together with limited followup treatment, can be effective.

Advanced computer technology applied to brain scanning has also shown evidence of alcohol-induced brain damage--even in the absence of obvious clinical signs.

In earlier reports, the significance of heredity--a biological predisposition toward alcoholism--was in doubt. A substantial body of animal and human research now leaves little question that heredity plays a role in susceptibility to some of alcohol's effects and in some individuals increases their likelihood of becoming dependent on it. The distinct possibility of identifying such potential alcoholics early may enable us to focus prevention efforts on those at high risk.

Our advances in knowledge have led to a measure of optimism in dealing with alcohol abuse. The 1990 Objectives for the Nation cited in this report reflect this. We are hopeful, for example, that, by 1990, 80 percent of high school seniors will feel, as only a third now do, that there is "great risk" in becoming intoxicated. It may be possible to reduce the percentage of problem drinkers of all ages by 20 percent. The increased health awareness in our country should facilitate achieving that goal. At the same time, we hope to attain reductions in alcohol-related accidents of over 20 percent and decrease cirrhosis mortality by 10 percent.

The risk of women's drinking while pregnant is now recognized by only three-quarters of women of childbearing age. Raising the consciousness of women to the point where at least 9 out of 10 are aware of the potential risk by the end of the decade is a realistic goal for our public information efforts.

While over half of Fortune 500 firms now have alcohol prevention and referral programs, we believe that a heightened awareness of the value of employee assistance programs will increase their numbers of 70 percent by 1990.

Building on the significantly improved epidemiological effort of the past decade, it should be possible by 1990 to collect far more comprehensive data on the impact of alcohol abuse on American society that will enable us to better monitor what is happening--and to modify our programs as we become more aware of changing national needs.

If this edition of Alcohol and Health provides some grounds for optimism, there is little basis for complacency. Alcohol continues to exact a fearsome toll. We sometimes forget that the cost of alcohol abuse to American society is higher than that for cancer, and at least equal to that for heart and vascular disease (Alcoholism and Related Problems: Opportunities for Research. Report of the Institute of Medicine of the National Academy of Sciences, Washington, D.C., 1980). The amount of our national resources devoted to reducing these costs is still modest compared with that earmarked for more "acceptable" disease. The moralistic stance of an earlier era, to that extent at least, is still with us. Many--perhaps most of us--continue to experience conflicts about our use of alcohol. As we resolve those conflicts, a more rational individual and collective approach becomes possible.

Robert G. Niven, M.D., Director
National Institute on Alcohol Abuse
and Alcoholism

Alcohol and Health—An Overview

Alcohol is undoubtedly the most widely used--and abused--drug in America. In 1981, the latest year for which figures are available, the equivalent of 2.77 gallons of absolute (pure) alcohol was sold per person over age 14. Translated into alcoholic beverages, this is about 591 12-ounce cans of beer or 115 bottles (fifths) of table wine or 35 fifths of 80 proof whisky, gin, or vodka.[1] However, Americans are far from equal in their drinking habits. In national surveys, a third of adults report they don't drink. Another third report drinking just over 2 drinks per week (0.21 oz. absolute alcohol/day), and the remaining third report consuming an average of 14 drinks per week. But such averages are deceiving--a tenth of the drinking population consume half the alcoholic beverages sold.

While drinking is nominally restricted to adults, it actually begins much earlier. By ninth grade, more than half (56 percent) of high school seniors responding to an annual 1982 national survey had tried alcohol. But by their senior year, more than 9 out of 10 (93 percent) had done so. Almost all seniors (90 percent) had drunk alcoholic beverages in the previous year. Two out of 5 seniors (41 percent) reported they had had five or more drinks--enough to become drunk--on a single occasion in the 2 weeks prior to the survey. Six percent reported drinking on a daily or near daily basis. High school drinking patterns over the 7 years sampled have changed very little. Male seniors drink more often than females and are more likely to do so daily.

A third (31 percent) of the high school seniors did not disapprove of drinking one or two drinks daily, although two-thirds (65 percent) felt that as many as four or five drinks per day would be harmful.

Defining Alcoholism and Heavy Drinking

Previous editions of this report, like this one, describe in detail many health and social consequences of alcohol abuse. These consequences can be summarized most succinctly by saying that there is much evidence--on many grounds--for concluding that alcohol used heavily is costly in human as well as economic terms. New evidence of that cost will be discussed here. But the question of how much must be used to produce a given effect is far more difficult to answer. Research on humans and animals indicates large individual differences in susceptibility to the drug.

When the term "alcoholic," "alcohol abuser," or "problem drinker" is used to designate an alcohol abuser, it must be kept in mind that these designations are somewhat less than precise. What is usually meant by an alcoholic is an individual who has been formally diagnosed as such or has (or has had) serious alcohol problems that meet implicit or explicit criteria of alcoholism, whether or not these have ever been formally diagnosed. It is hoped that, in this report, context will clarify meaning. Similarly, the term "heavy use" sometimes means use that is statistically more frequent than is true of American users generally (as in: "The heaviest using third of the population consume an average of 14 drinks per week."). More often, it is used to indicate a level at which pathological (or adverse behavioral) changes occur more frequently. Some types of episodic or binge drinking may fit neither definition of heavy use, but may nevertheless have serious implications (e.g., drunk driving).

While we have indicated the drink equivalent of a particular amount of absolute alcohol, in reality typical drinks are by no means uniform, and we are forced to rely on rough approximations. As in describing other areas of real life (e.g., smoking habits), we are obliged to accept a certain lack of precision. But within those limits, meaningful observations are possible, as this and earlier reports demonstrate.

Alcoholism and Heredity

Is alcoholism inherited? New evidence concerning genetic susceptibility to alcoholism is

[1] Assuming 0.6 oz. absolute alcohol = 1.5 oz. 80 proof spirits = 5 oz. table wine (12 percent alcohol) = 12 oz. beer (5 percent alcohol).

one of the exciting developments in recent research. The belief that alcoholism somehow "runs in families" is an old one. But growing up with an alcoholic parent as a role model has been the traditional explanation for the higher than normal rate of alcoholism in children of alcoholics. Evidence that alcoholics' children, despite having been raised by nonalcoholics, still have a higher rate of alcoholism is persuasive that genetics plays an important role. Moreover, specific biochemical and physiological characteristics in which heredity appears to be important have recently been identified in alcoholics.

A pioneering study of alcoholics who had half-siblings (i.e., brothers or sisters with whom they had only one biological parent in common) found that half-siblings who were also alcoholic were three times more likely to have had an alcoholic natural parent than the nonalcoholic half-siblings.

Research on children adopted at an early age also helps to clarify the role of heredity and environment. Researchers studied a matched sample of natural sons of alcoholics who were then adopted by others, comparing them with the natural sons of nonalcoholics who were also adopted. Both groups had been raised by nonalcoholic adoptive parents. The alcoholics' sons proved to be three times more likely to become alcoholics than the sons of nonalcoholic parents. When the sons of alcoholics were compared with their brothers who had remained in their alcoholic families of origin, the two groups had the same rates of alcoholism, a finding that heredity plays an important role in the development of alcoholism.

Although too few females were considered in the above studies to draw any conclusions about a genetic factor in women alcoholics, a more recent study of adopted women found that those whose natural mothers were alcohol abusers were four times more likely to become alcoholics than those whose mothers were not. Alcoholic fathers did not seem to have the same effect on their daughters. Interpreting this study is complicated by the possible role of the mothers' alcohol use while pregnant in affecting their daughters' later alcohol problems. While it is the first study to suggest a biological predisposition in women alcoholics, there is no way of knowing whether the predisposition is on an in utero developmental basis or a hereditary basis--or both.

A more recent study identified a male limited form of alcoholism where sons of alcoholic fathers are at ninefold higher risk for developing alcoholism themselves.

While the research just described has stressed the importance of genetics in the eventual development of alcoholism, it is certainly not a simple matter of "nature vs. nurture." Other studies suggest that with a genetic susceptibility toward becoming alcoholic, the additional factor of nurturance by an alcoholic parent doubles the chances of the child's becoming alcoholic. But for many, probably most, alcoholics, genetic factors are not apparent in their immediate family's history. However, this does not rule out heredity. Since studies have not been made of multiple generations, there is no way of knowing whether such a biological tendency was present in earlier generations.

Animal research in which systematic inbreeding for several generations has been done clearly indicates the important role of genetics in determining individual susceptibility to many of alcohol's biological effects. Strains of animals can also be selectively bred to prefer drinking alcohol while other strains do not.

Assuming that some inherited tendency increases the likelihood of a person's becoming alcoholic, there are many ways in which it might operate. To name a few: The individual could be more sensitive to certain kinds of stimulus overload, and alcohol may blunt this sensitivity--a mode of self-medication. The central nervous system might neurochemically function in a way that makes it more readily dependent on the drug. It could also account for a more rapid development of tolerance (the need for greater amounts to produce a given effect) and physical dependence. There is some evidence for all of these and other mechanisms as well.

Studies of human twins suggest that as much as half the variation in the rate at which alcohol is eliminated from the body may be genetically determined. The other half is probably related to how alcohol and other drugs are used, diet, and other personal habits. Twin studies also indicate genetically based variation in susceptibility to such medical complications as cirrhosis of the liver and alcohol-induced mental disorders.

Researchers have recently found that one form of the genetically determined liver enzyme aldehyde dehydrogenase is absent in many Orientals. This likely accounts for the higher rate of facial flushing observed after drinking among many of these individuals. The facial flushing is often accompanied by nausea, vomiting, and a drop in blood pressure. These unpleasant symptoms are similar to the reaction that occurs when a person taking

disulfiram consumes alcohol. Such built-in negative responses to alcohol may partially explain why individuals from similar backgrounds often differ so widely in their alcohol consumption.

The certainty that heredity plays a significant role in the development of harmful drinking behaviors and in affecting individual sensitivity to alcohol's injurious effects offers the possibility of better defining biological subtypes of alcohol abusers. If the initial optimism about finding biochemical markers is justified by further research, it may be possible to identify potential alcoholics early--before they develop serious alcohol problems or alcoholism.

Alcohol and the Brain

Alcohol's effects on the brain are among its most seductive--and destructive--properties. Its pleasure-giving potential, along with many of its behavioral hazards, has been recognized since antiquity. Its natural occurrence through spontaneous fermentation probably makes it our most ancient mind-altering substance. But it is only very recently that we are beginning to understand the complexity of alcohol's effects and their underlying neuroanatomical and physiological basis.

Effects of Alcohol on Skilled Performance

Amounts often drunk socially (two or three drinks in an hour) can cause significant impairment in the skills required in driving, flying, and other complex performance. Recent evidence also indicates that time of day can make a difference in how seriously one's performance is affected. Decrements typically persist for many hours after drinking in the evening. Alcohol combined with fatigue has a more pronounced effect than either alone. Recent evidence also suggests that alcohol and tobacco have a greater combined effect on auditory alertness than when used separately.

Overall, there is compelling evidence that alcohol alone and in combination with other commonly used drugs has serious effects on many kinds of performance. The decrements are generally dose-related--the greater the amount consumed, the greater the impairment that results. Further documentation of this can be found in earlier editions of this report.

Alcohol and Brain Damage

Chronic brain injury caused by alcohol is second only to Alzheimer's disease as a known cause of mental deterioration in adults. Many of the symptoms--loss of ability to think abstractly, speech difficulty, and decreased coordination--are similar in the two types of disease. Both groups of patients show brain atrophy (shrinkage) and similar abnormalities in brain electrical functioning. However, Alzheimer's disease is invariably progressive, whereas alcoholic mental deterioration is not. If the patient stops drinking, the deterioration is arrested and substantial recovery can occur.

(Even in alcoholics without obvious evidence of mental deterioration, CAT scans--computerized techniques for visualizing and measuring the brain--have revealed abnormalities). Another advanced computerized method (average evoked response or AER) measures the response of the brain to light and sound stimulation. Recent work indicates that alcoholics respond differently than do nonalcoholic persons. Alcoholics are more sensitive to the stimulation. One theory is that their sensitivity leads them to drink in an effort to reduce their stimulus overload. Possible evidence of this is the recent discovery that those with family histories of alcohol use--even though they were not themselves alcoholics--were different in their AERs from those who had no alcoholics in the family. If this finding is confirmed, it may provide another means for early identification of those at risk of becoming alcoholics.

Other advances in brain measurement have found that alcohol alters brain activity in parts of the brain involved in memory, emotion, and higher level functioning. Microscopic study of the brains of patients who have died with Korsakoff's syndrome, an alcohol-induced disease characterized by severe memory loss and impaired learning, has disclosed brain injury near nerve pathways involved in these functions. These brain lesions are very like those found in patients who have died of acute vitamin B_1 (thiamine) deficiency, possibly indicating that a similar vitamin deficiency occurs after chronic heavy alcohol use.

Debate took place in the past over whether the brain injury found in alcoholics is the result of alcohol as such or of the dietary deficiencies that are so common in advanced alcoholism. It is now known that alcohol itself injures brain tissue, although the combination of excessive drinking and poor diet may accelerate the process.

Neurochemistry--the study of minute quantities of chemicals in the brain that govern how nerve cells transmit their messages--is also advancing our understanding of alcohol. But the effects of the drug on these neurotransmitters is not simple. They seem to vary depending on the part of the brain involved as well as the dose.

Dose-related opposing effects have been found on the neurotransmitter norepinephrine. At low doses alcohol increases norepinephrine release, but at higher doses release of the chemical is inhibited. This seems to correspond to the everyday observation that alcohol is initially stimulating in small amounts but has a depressant effect as more is consumed.

Another neurotransmitter, GABA, inhibits neuronal firing and can control the tendency toward certain types of convulsions. Animal research indicates that animals chronically given alcohol have a reduced number of receptor sites for GABA. This suggests that GABA may play a role in the seizures often seen in alcoholics.

Other research, on the neurocellular level, is probing alcohol's effects on cell membranes. It may explain how tolerance for alcohol--its decreased effect when used regularly--develops and the neurocellular basis for physical dependence.

Earlier research has found that alcohol can affect parts of the brain involved in reward or pleasure. There is now heightened interest in other mechanisms by which alcohol and similar dependency-producing drugs operate. Naturally occurring opiate-like compounds have been found in the brain. Both these chemicals and externally derived opiates seem to have similar sites of action--the opiate receptors. Chronic doses of alcohol in test animals may alter the function of these opiate receptors. This finding has led scientists to speculate that alcohol and other psychoactive drugs may act similarly in the brain. Some support for this theory comes from the observation that narcotic antagonists--drugs that can block the effects of an opiate by occupying opiate receptor sites--also block some, but not all, of alcohol's effects.

Another provocative preliminary hypothesis is that a group of chemicals called tetrahydroisoquinolines, or TIQs, may play a role in habitual heavy drinking. TIQs are formed when alcohol is metabolized. In some animal experiments, when these chemicals were injected into the brains of animals, their preference for alcohol increased significantly.

All of these preliminary neurophysiological observations fall short of adequately explaining the action of alcohol. Additional research is needed to sort out some of these conflicting--and still clearly incomplete--explanations.

Other Health Hazards

Even a casual observer notices some of the effects of heavy drinking on the brain and the complex behavior it controls. But there are other, more insidious, consequences for other parts of the body as well. And many of these are not apparent even to knowledgeable drinkers.

The Digestive Tract

Cancers of the mouth, tongue, pharynx, and esophagus are more common in alcoholics than in nonalcoholics. While the exact cause or causes are unknown, alcohol's direct irritation of mucous membranes is well established. This, combined with the known carcinogenic properties of tobacco so often smoked by heavy drinkers, is likely to be jointly responsible. Vitamin A and B deficiencies because of poor diet and/or alcohol's interference with the vitamins' absorption may also play a role. Animals that are vitamin A deficient are known to be more susceptible to skin, mouth, and esophageal cancers.

Alcohol alters stomach acid secretion, which along with its irritating gastric lining probably accounts for the stomach problems so common in alcoholics. It weakens the stomach wall, making it more susceptible to bleeding. The use of aspirin by drinkers may increase the likelihood of bleeding from the already weakened wall, sometimes leading to hemorrhage.

Alcohol has multiple effects in the intestines. It impairs vitamin absorption, is an irritant, and results in increased gastrointestinal motility. This often leads to diarrhea in heavy drinkers, which may contribute to their poor nutritional state.

Chronic pancreatitis is common in alcoholics. Seventy-five percent of the cases in the United States are believed to occur in alcoholics. Although pancreatitis often results in abdominal pain and vomiting, half the alcoholic population show alteration in pancreatic function without obvious symptoms. Recent evidence suggests that alcoholics may have

more of a specific genetically determined antigen--a chemical that activates the immune system, which suggests a genetic mechanism behind the vulnerability to this disorder. Pancreatic cancer is also twice as frequent in alcoholics--75 percent of those who contract the disease are moderate to heavy drinkers.

Perhaps the best known effects of excessive alcohol use are those on the liver. These range from fatty liver, the most common--and reversible--problem, to cirrhosis, which is life-endangering and irreversible. While it was once thought that liver damage could be averted by an adequate diet, it is now known that damage occurs regardless of how nourishing the heavy drinker's diet is. Alcoholic hepatitis also results from heavy drinking. The inflammation and later destruction of liver cells from this disease kills 10 to 30 percent of those who develop it. Alcoholic cirrhosis is the most dangerous consequence to the liver from drinking, causing at least 11,000 deaths annually in the United States.

Alcohol and the Heart

Alcohol when used heavily may have detrimental effects on the heart. Cardiac myopathy--damage to the heart muscle--often occurs after 10 or more years of heavy drinking. Symptoms of this disorder range from chronic shortness of breath and ankle swelling to heart failure. Degenerative changes in heart muscle cells can be seen with the electron microscope. If the damage is not too extensive, recovery is possible, although it may require 5 or more years of abstinence.

Alcohol also interferes with the heart's ability to contract. Heart beat irregularities (cardiac arrhythmias), which can lead to heart failure, are common in alcoholics. Two ounces of whisky drunk by an individual who already has heart disease can suppress the heart's pacemaking abilities.

Effects on Other Muscles

The effects of alcohol on muscle tissue are not confined to the heart. Muscular weakness and severe pain from muscle cramping are fairly common in heavy imbibers. Mild symptoms of these myopathies, which may not be severe enough to come to medical attention, occur in about a third of alcoholics. Alcohol also affects involuntary smooth muscle contractions.

Alcohol and the Blood

Excessive drinking causes blood abnormalities. Both enlarged red blood cells and anemia are produced. These are probably the combined result of vitamin deficiency, alterations in fat metabolism (because of liver damage), and other still unknown or poorly understood mechanisms. Abnormally large cells are so common (found in 90 percent of alcoholics) that a measure of this, the mean corpuscular volume or MCV, has been suggested as a means of detecting alcoholism. Four or more months of abstinence may be required before the MCV returns to normal.

Many alcoholics also have reduced white blood cell counts. These cells play an important role in the body's immune response. A diminished immune response has now been reported in alcoholics. The higher rates of infectious disease common in this group are probably attributable to this lowered resistance.

Alcohol and Sexuality

Alcohol interferes with male sexual functioning. That was known in Shakespeare's time--and probably before. But recent research provides both confirmation and an explanation. Impotence and/or reduced sexual drive are found in from 70 to 80 percent of alcoholics. The same percentages have been reported to show testicular atrophy and infertility. Alcoholics have much lower levels of the principal male hormone testosterone than do nonalcoholics, along with increased levels of female hormones. Because of this, 50 percent of male alcoholics develop feminine pubic hair patterns, and 20 percent have breast enlargement.

Like other effects of alcohol, these changes in sexuality were once believed to arise from liver injury. More recent evidence clearly indicates that alcohol reduces testosterone levels and causes direct gonadal injury. It also affects sexual functioning indirectly through its impact on the brain's hypothalamus and the pituitary, the so-called master gland. Recent research suggests that the increase in estrogen levels found in alcoholic men is also partly due to adrenal changes. The adrenal glands produce estrogen precursors--chemicals from which estrogens are later formed, although the mechanisms involved are not yet known.

The alcoholic female's sexuality is also affected by her drinking. Severe gonadal fail-

ure--an inability to produce adequate quantities of female hormones--leads to loss of such secondary sexual characteristics as fat deposits in the breasts and other parts of the body, reduced (or absent) menstruation, and infertility. As with men, the control of hormone production by the brain and the pituitary gland is affected.

Alcohol and Pregnancy

Clinical and experimental research over the past decade underscores the threat to the developing fetus that maternal alcohol misuse represents. The term fetal alcohol syndrome (FAS), first used 10 years ago to describe a set of symptoms in the newborn infant believed to be caused by heavy maternal alcohol abuse, has recently been more carefully standardized. The new standard demands that three kinds of characteristics be found in the newborn to justify being classified as a case of FAS: (1) growth retardation before or after birth, (2) abnormal features of the face and head such as unusually small head circumference and/or flattening of facial features, and (3) evidence of central nervous system abnormality (e.g., mental retardation, abnormal behavior, etc.).

Other birth anomalies are regarded as alcohol related if there is evidence of heavy or frequent maternal drinking during pregnancy and if the specific anomalies occur in greater frequency, after control for confounding variables, among the children of heavier than lighter drinkers or abstainers. Some studies suggest a risk for outcomes including decreased birth weight and increased spontaneous abortion at levels of alcohol consumption as low as two drinks per day, although some investigators question whether these self-reported consumption levels are not in actuality higher. Isolated instances of heavy drinking may also pose significant hazard.

Women's alcohol use during pregnancy has been described by one research group as "the most frequent known teratogenic cause of mental retardation in the Western World." However, the prevalence of fetal alcohol syndrome or of other alcohol-related birth defects is not easy to specify. Moreover, since heavy drinkers often underestimate (or underreport) levels of drinking, it is difficult to be certain how much alcohol consumption is required, at what point or points in pregnancy, to produce abnormalities. Because developing fetuses probably differ in their sensitivity to alcohol as well, the pattern of alcohol use that will result in congenital anomalies cannot be specified with precision.

One somewhat encouraging finding is that many women who usually drink heavily markedly decrease their drinking while pregnant. Such a reduction might be expected to decrease the risk of congenital defects.

Current estimates are that FAS affects somewhere between 1 and 3 births per 1,000, but other alcohol-related birth defects probably add significantly to that number. A recent calculation suggests that 5 percent of total birth defects may be alcohol related.

Animal research, which can be more carefully controlled than that on humans, leaves little doubt that alcohol ingestion during pregnancy has serious consequences. Birth defects closely resembling those found in humans have been produced in many animal species. Scientists who administered two doses of alcohol to mice on one day early in pregnancy (an animal model resembling human binge drinking) found abnormal facial features in offspring like those reported in human FAS. Extensive animal--and human--findings amply justify discouraging women from drinking while pregnant.

Lowered birth weight is the most consistent result of alcohol use during pregnancy. Since low birth weight is associated with more frequent neonatal deaths and is frequently associated with mental retardation and neurological defects, this finding is important.

Several studies have found low IQ and motor development scores related to maternal alcohol use. Most recently (1983), 4-year-olds whose mothers drank during their gestation were found to have decreased attention spans and slow reaction times. Children with FAS and animals prenatally exposed to alcohol have been found to show hyperactivity.

Paternal Drinking

Although it is known that long-term alcohol use by men can lead to reduced sperm counts, decreased sperm motility, and higher rates of sperm abnormalities, there is no evidence from either animal or human studies that heavy alcohol use leads to congenital defects in the children of such men.

Adverse Social Consequences

Alcohol abuse plays a role in many kinds of social problems. In some--traffic accidents,

for example--what is known about alcohol's effects on complex skills makes it reasonable to ascribe a causal role to the drug. In other problems--child and spouse abuse, for example--excessive alcohol use is probably not the primary cause although it may contribute significantly, perhaps by reducing inhibitions that might otherwise curb expression of anger.

Traffic Accidents

Traffic accidents are the fifth leading cause of death in the United States and its leading cause among those under age 35. In the latest year for which data exist (1981), such tragedies killed 49,000 and permanently disabled another 150,000 persons. The consensus is clear--alcohol is responsible for up to half of these tragedies. A review of 23 studies found a third or more of drivers in fatal accidents had blood alcohol concentrations (BAC) above the usual legal standard for drunk driving of 0.10 percent. Five or six drinks consumed in the 2 hours before driving can cause this level in a 155-pound person. Drivers with blood alcohol concentrations above 0.10 percent have been estimated to be 3 to 15 times more likely to have a fatal accident than nondrinking drivers. Other estimates have concluded that even lower BAC levels--from 0.05 to 0.099 percent--increase the risk from 1.25 to 3.25 times. This is the level that results when a 155-pound person has had three to four drinks or a 120-pound person as few as two to three drinks within 2 hours. Unfortunately, many people are not aware of these risks. A recent Massachusetts survey found that 17 percent of respondents believed the fiction that you can have six or more drinks without becoming too drunk to drive. (Six drinks in a 155-pound person would result in a BAC above 0.10 percent, even if the drinks were consumed during a 3-hour period before driving.)

Pedestrians who have been drinking also have a much higher risk of being injured or killed in a traffic accident than do nondrinkers. In one recent study, more than a third (36 percent) of injured pedestrians and nearly half (45 percent) of those who died from being struck by a motor vehicle had blood alcohol concentrations above 0.10 percent. Only 13 percent of a control sample of uninjured pedestrians passing the same accident sites at a similar time had that high a BAC. As with motorists, the higher the blood level, the higher the risk of accident involvement. Compared with that of the nondrinking pedestrian, the risk of being hit was twice as high at blood levels above 0.10 percent, five times higher if the BAC was above 0.20 percent.

Industrial Accidents

Less is known about the relationship of alcohol to industrial accidents than to traffic accidents, although such a connection is predictable. A 1982 Maryland study of workers who died in job-related accidents found that 11 percent had BACs above 0.08 percent. While this may not be nationally representative, it indicates a relationship that should be further examined.

Other Accidents

It is hardly surprising that the heavy imbiber is at greater risk in other types of accidents as well. Accident statistics are consistent with this expectation. Alcoholics are 5 to 13 times more likely to die from falls than nonalcoholics. Alcoholics are also much more likely to die in fires--a tenfold increase over nonalcoholics. Heavy drinkers had 2.7 times the accidental death rate (omitting traffic accidents) of other Kaiser-Permanente members during a 10-year followup period. While such statistics do not prove that alcohol played a direct role in the particular hazard, the presumption cannot be dismissed.

Alcohol and Crime

Although many statistical associations have been made between alcohol use and criminal behavior, a direct causal link is more tenuous. One of the earlier homicide studies (1958) found that either the murderer or the victim had been drinking in two-thirds of the slayings reviewed. Subsequent research has also found that a majority of murderers, their victims, or both had been drinking prior to the crime. Whatever the role of drinking in such studies, it is confounded by such factors as a failure to control for age, sex, and race, all of which are related to both violence and drinking. The most that can be concluded is that alcohol is a contributing cause but is probably only one of several factors involved.

Rape

The role of alcohol in rape is even more difficult to assess. Not only is rape very underreported--authorities agree that only a

minority of attacks are reported--but intoxication may be offered as an excuse or extenuating circumstance by the rapist. Studies of rapists, however, indicate that they often drank heavily prior to the crime, and that their rate of alcoholism is two to three times that of the general population. Whether alcohol plays a disinhibiting role, or serves as a justification for the behavior, or plays some other part is unclear.

Alcohol and the Family

Alcohol abuse undoubtedly affects family life. It is noteworthy that a third of persons interviewed in a 1982 survey felt that alcohol caused problems in their families. But the precise ways in which it does so are more difficult to document. The rate of separation and divorce among alcoholics is seven times that of the general population. Two out of five domestic relations court cases involve alcohol.

While few doubt that heavy drinking plays some role in family violence and the abuse of spouses and children, just how and to what extent is again hard to specify. Most studies report that alcoholism or excessive drinking is involved in about half the cases of spouse abuse. As with rape, drinking may be used as an excuse for the violence involved. Early reviews of child abuse have described associations between it and alcohol in as many as 38 percent of cases. However, a recent review has concluded that alcohol involvement in child abuse is no higher than in the general population.

A 1983 review of the effects of parental alcoholism on children indicates that they are more likely to have school problems and to display antisocial behavior. Other studies report that such children have less self-esteem, more anxiety symptoms, more aggression, and more psychosomatic symptoms.

Alcohol and Suicide

Given the high rate of depression in alcoholics, it is not surprising that they have a high rate of suicide. But here, too, it is unclear whether the depression contributes to the drinking and suicide, or the alcohol use causes the depression and ensuing self-destruction. Nevertheless, as the Fourth Special Report noted, as high as four out of five of those who attempt suicide had been drinking at the time. Alcoholics commit suicide from 6 to 15 times more frequently than the general population.

Economic Costs

General agreement exists that alcohol abuse results in lost work productivity and an increase in industrial accidents. In one study of railroad companies, problem drinkers had twice the absenteeism of other employees. Much less is known about the costs associated with episodic drinking on or off the job as it affects work performance.

Estimating the cost of alcohol abuse to American society is difficult. Many of the variables that should be taken into account are simply not known with sufficient accuracy. But even making very conservative assumptions about these factors, a recent calculation places the annual national loss at about $49.4 billion. The bulk of this amount--$36.8 billion--represents the value of lost productivity. The cost of various kinds of medical care for alcohol-related illness and injury totals $6.4 billion. The remaining $6.2 billion includes such added costs as traffic accidents, fires, crime, and other miscellaneous losses attributable to alcohol.

Perhaps the highest cost is the incalculable pain and misery associated with alcohol abuse for the abusers, their families, and the larger society. There is no disagreement that those costs are profound.

Treatment Trends

A basic problem in treatment is deciding just who is an alcoholic and just what is alcohol abuse. Failure to agree on definitions is the basis for much of the confusion regarding the exact prevalence of alcohol abuse and its implications. The latest revision of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-III) represents an important advance in conceptual and diagnostic clarity. Using a multidimensional matrix, it takes into account alcohol-induced symptoms, psychosocial stress, the patient's level of adaptive functioning, and related personality disorders. It is hoped that the new manual will ensure uniform standards that will in turn permit increased comparability of treatment and research findings.

A related development in diagnosis is the improvement in relevant sections of the International Classification of Diseases (ICD) resulting from collaborative effort between the U.S. Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) and the

World Health Organization (WHO). Central to the WHO approach is the concept of a dependence syndrome, an interrelated cluster of cognitive, behavioral, and physiological symptoms.

One of the most promising new developments is the emergence of a group of biochemical markers to assist in identifying alcoholics. While each of these tests has limitations, several studies have now found that a profile of multiple blood tests can quite accurately differentiate alcoholics from nonalcoholics.

The new Munich Alcoholism Test uses both clinical signs and symptoms noted by the examining physician. When combined with self-reporting instruments and the biological marker approach, such testing promises to more usefully discriminate between different types of alcohol-dependent patients. In preliminary trials of this approach, psychosocial problems were most evident in young abusers, with clinical signs and symptoms more common in older alcoholics.

Early Intervention

Early identification through the sophisticated techniques now available offers the possibility of early intervention. And there is now increasing evidence that it works. Even a 35-minute counseling session in a general hospital setting has been found to reduce drinking in a significant number of newly identified problem drinkers who were followed up for 1 year.

A recent Swedish study using a biochemical marker--elevated GGTP scores--to identify heavy drinkers has also found that early intervention can be valuable. Those identified were told their GGTP results and their significance. They were then repeatedly retested, given feedback on their progress, and encouraged to moderate their drinking. The group had lower work absenteeism, fewer hospitalizations, and a lower death rate during the 6-year followup.

In France, a combination of two biochemical tests and a clinical examination is now being used on a nationwide scale to detect early alcohol abuse in industrial, health care, and court settings. When a problem is found, the individual is referred to local early intervention clinics for care. The system, which has yet to be evaluated, illustrates the feasibility of large-scale intervention.

Work-based alcoholism treatment intervention as an alternative to disciplining the worker has also shown definite promise. Several studies have found that it works as well as voluntarily sought treatment when measured by abstinence and improved job performance.

Detoxification

Detoxification--the process of withdrawing the alcohol-dependent patient from alcohol and controlling his or her withdrawal symptoms--has traditionally been done in a hospital setting. In recent years, partly because of the high cost of in-hospital detoxification, other settings have been tried. Although these alternatives have not been systematically evaluated, a review of the evidence suggests that detoxification can be done humanely, safely, and efficiently in nonhospital settings. It may, however, be important to develop clear criteria of what types of alcohol abusers are most successfully treated by the new alternatives.

Treatment Benefits

A number of studies testing the feasibility of treating alcoholics through medical insurance plans have now been completed. All have found that alcoholics and their families are initially more expensive to treat, as they require more care than those without alcohol problems. However, following treatment for alcoholism, demand for services drops, and the treatment is unquestionably cost-effective in reducing total medical expenses. The median reduction in sick days and accident benefits was 40 percent in one review of 12 programs.

Research comparing inpatient and outpatient treatment settings has not found significant differences in treatment outcome. Since patients are not usually randomly assigned to each type of setting, it is not yet known whether differences in the types of patients normally sent to these two settings are important. (Seriously ill patients with medical complications may still be more appropriately treated in a hospital.)

Client-Program Matching

The problem of developing programs suited to special populations such as women, ethnic minorities, and the elderly has become important. As this and earlier reports indicate, groups such as Native Americans have much higher rates of illness and death from alcohol-related illness than does the general population. It is critical that treatment programs

be designed to overcome cultural, economic, and other barriers that deter some groups from seeking treatment. A survey of California facilities found that women alcoholics were less likely to seek treatment if programs lacked child care and aftercare arrangements and professional staff. More and more programs are being designed to meet these and other needs of special populations.

Treatment Approaches

Several experimental approaches to treatment have been extensively evaluated since the Fourth Special Report. Aversion therapy, which links the sight, smell, and taste of alcohol with a nausea-producing drug, appears to be effective with stable, well-motivated alcoholics, while the same approach substituting electrical shock appears not to be. A related technique--covert sensitization--that pairs verbally induced nausea with imagined alcohol consumption produces greater improvement than insight-oriented therapy, based on a 4-year followup.

A recent study of disulfiram (Antabuse) not discussed in the Fourth Special Report found the drug slightly more effective in producing abstinence after a year than a vitamin B preparation. Another study found that additional training in role playing, communication, and stimulus control along with the use of disulfiram was effective with married clients, but not with the unmarried. Further training in drink refusal, social skills, muscle relaxation, and job and recreational counseling for the single group raised their abstinence levels, however. Closely supervised use of disulfiram in an industrial setting was effective in reducing absenteeism.

Traditional psychotherapy has been found not to be generally effective with alcoholics, but may be useful with some types. Family therapy is also being tried, although it has not yet been fully evaluated.

Early findings suggested that some "definitely alcoholic" clients were capable of drinking moderately 6 months after treatment and up to a year later. However, a followup 4 years later has found that those who were abstinent at 18 months were less likely to have drinking problems at 4 years than those who drank moderately at 18 months.

Patients affiliated with such aftercare groups as halfway houses and Alcoholics Anonymous have been found to have better therapeutic outcomes than those who remain unaffiliated.

Prevention

Alcohol abuse prevention is becoming more important as awareness grows that alcohol problems are present in the entire drinking population. While problems occur at lower rates in groups that drink less, they are rarely totally absent.

There is little question that alcohol education programs can increase knowledge concerning alcohol and may also alter attitudes toward the substance. But the question of the extent to which they modify actual drinking behavior is not so easily answered. Even when such changes have been assessed--and most programs have not tried to do so--they are difficult to interpret. Changes in economic conditions, minimum ages at which drinking is permitted, and law enforcement policy are all likely to overshadow program effects.

A 1982 study found that teaching 7th through 10th graders about alcohol improved their knowledge and also reduced their use. A recent review of prevention programs emphasizes that improved decisionmaking is likely to lead to a reduction in pro-drinking attitudes, although it is overly optimistic to expect significant use reduction based on such limited interventions.

Nontraditional programs emphasizing interactive learning, which involves students in the actual design of the prevention program, seem to be most successful in altering attitudes and possibly drinking behavior.

Intervention--between 6th and 9th grades--to teach youngsters to develop resistance to later use of alcohol (and tobacco) is a promising prevention strategy, although it has not yet been followed up with longitudinal studies.

Because the college years are important in developing long-term drinking habits, a number of programs have been directed toward these students. Improvements in knowledge occur and there is evidence that attitudes shift, but no changes in actual drinking have been found.

Increased sophistication is evident in programs tailored to meet the needs of women (especially during pregnancy), minorities, and other special populations such as the elderly. These new programs need to be tested for effectiveness.

Mass media campaigns are probably too weak an intervention to significantly alter drinking behavior unless they are closely coordinated with local education and training efforts. However, they can be useful in generating heightened interest in alcohol prob-

lems and in mobilizing community resources to deal with the problem.

Lowering alcohol consumption levels is associated with reduction in a number of adverse effects of drinking such as alcohol-related traffic accidents (especially by youth) and diseases such as cirrhosis of the liver. Some effective efforts, documented through research, are:

- Increasing taxes on alcoholic beverages
- Increasing the legal age for purchase of alcoholic beverages
- Altering the number and location of outlets for purchase of alcoholic beverages.

Future Directions

New directions are evident in many parts of this report. Among the most promising are improved early identification of potential problem drinkers and alcoholics and expanding present basic knowledge of just how and why alcohol abuse is so destructive. Basic research may result in developing strategies that reduce the likelihood of those who are genetically more vulnerable becoming alcohol dependent. It may also enable them to drink moderately with less hazard.

New evidence of the serious threat alcohol poses to the developing fetus argues persuasively for enhanced efforts at preventing maternal drinking by making women more fully aware of the risk. The evidence that many individuals are many times more vulnerable to alcohol's destructiveness demands that better prevention and treatment be developed for those at high risk. Better targeted prevention efforts are also implicit in early detection of genetic vulnerability to alcohol through the use of biological markers.

Treatment offers many opportunities for increased innovation. One is to tailor programs to fit the needs of different types of clients. Many approaches that have been used with reported success have not been adequately evaluated. The cost-effectiveness of early intervention in health maintenance organizations and industry argues for more aggressive efforts by both.

Alcohol problems have plagued most societies throughout history. But never before have we had as much basic knowledge as we now possess, with the promise of still greater understanding to come.

Chapter I

Epidemiology of Alcohol Abuse and Alcoholism

Epidemiological research is useful in identifying many of the social, environmental, behavioral, and biological factors associated with alcoholism and alcohol abuse. New insights and understanding of these factors are complicated by the lack of standard and uniformly applied definitions. Terms such as alcohol abuse, alcohol misuse, problem drinking, alcoholism, and alcohol dependence are often used interchangeably. The development of uniform operational definitions should lead to continued advances in the epidemiology of alcohol-related conditions. Meanwhile, researchers and policymakers must rely on current terminology and the best data available to understand the problems associated with alcohol abuse and alcoholism. The data presented here indicate the scope and magnitude of alcohol abuse and alcoholism in this country and provide a framework for discussing the effects of the excessive consumption of alcoholic beverages.

Consumption of Alcoholic Beverages Measured by Alcohol Sales

Sales of alcoholic beverages are often used as an indirect measure of alcohol consumption. But per capita consumption figures based on sales and excise tax data do not take into account the amount of alcohol consumed in one State but purchased in another, the amount of alcohol purchased but not consumed in any given year, sales of alcohol that go unreported, and the consumption of illegally produced alcohol (e.g., moonshine).

Figure 1 shows the estimated per capita alcohol sales for beer, wine, distilled spirits, and the three beverage types combined. The estimates are expressed in gallons of absolute alcohol per person, per year, for the United States. For statistical purposes, this population is defined as the estimated population 15 years of age or older for years up through 1969, and 14 years of age or older for years 1970 through 1981. For 1981, the average estimated consumption is 2.77 gallons per year or approximately 1 ounce of absolute alcohol per day for each person in this population. Fifty-one percent of the absolute alcohol consumed in 1981 was beer (1.40 gallons per person), 36 percent distilled spirits (1.01 gallons per person), and 13 percent wine (0.35 gallons per person).

Figure 2 displays estimated per capita consumption in 1981 for the three alcoholic beverage types combined for each State and the District of Columbia (NIAAA 1982a, d, e). This map indicates that substantial variation exists across States in quantity of alcohol sold. Statistical data for each State also indicate considerable variation in the relative sales of each type of alcoholic beverage. A number of factors may influence the variation in beverage sales and apparent per capita consumption across States, including:

- Difference in State taxes for each type of beverage
- Difference in the legal drinking age within each State
- Differences in State legislation regarding the location, type of outlets, and hours of operation for selling alcoholic beverages
- Differences in cultural and social habits across geographic regions.

U.S. alcohol per capita sales have increased approximately 35 percent since the early 1960s, but only 7 percent since 1971. While estimated per capita sales of beer rose 22 percent and of wine rose 13 percent, sales of distilled spirits have dropped 10 percent since 1971. Considerable variation in sales rates occurs among States, e.g., a decrease of 17 percent in the District of Columbia and an increase of 36 percent in Hawaii. These data

must be interpreted cautiously, however, because the States are differentially affected by such factors as drinking age, degree of urbanization, tourism, and out-of-State purchasers.

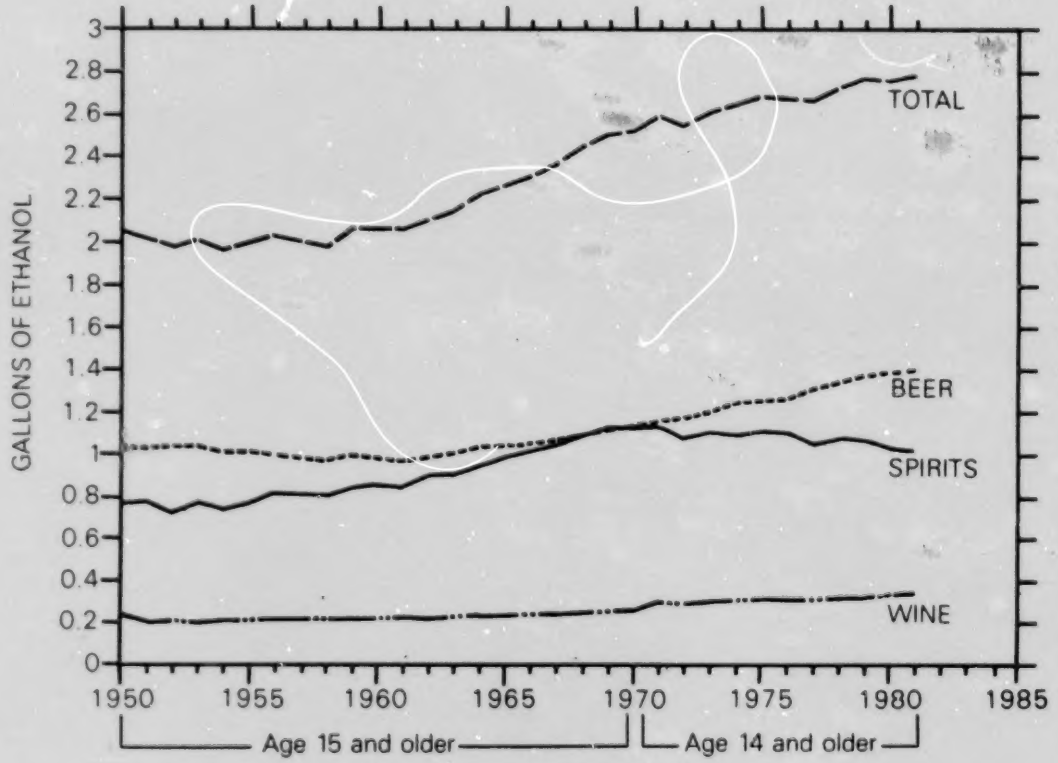
Surveys of Self-Reported Consumption Among Adults

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has sponsored a series of national surveys that characterize the self-reported drinking patterns of the U.S. adult population. Results across these surveys conducted in the 1970s are similar. Approximately one-third of the adult population described themselves as alcohol abstainers (consumed not a single drink in the year prior to the survey). Another third described themselves as light drinkers (consuming up to 0.21 ounces of absolute alcohol per day on the average), while the remaining third were moderate (0.22-0.99 ounces) or heavier drinkers (1.0 ounces or more), the latter (heavier drinkers) consuming the equivalent of approximately two drinks or more every day.

Men drink significantly more than women, and younger adults more than older adults (see figure 3). The most recent national survey (1979) confirms these sex and age variations. In addition, the 1979 data indicate that abstaining from alcohol is less common in the New England and Pacific regions and more common in the South, and that the proportion of abstainers falls as income rises and years of schooling increase.

Findings from other national household surveys also confirm that alcohol consumption

Figure 1. Apparent U.S. Consumption of Alcoholic Beverages in Gallons of Ethanol Per Capita 1950-1981



SOURCE: Data from NIAAA 1982b,e,f

is greater among younger adults than among older adults. During the years 1974 through 1982, the annual prevalence of alcohol use among younger adults, 18 to 25 years old, was approximately 22 percent greater than among adults 26 years and older. Overall, the annual prevalence of alcohol use reveals a slight but gradual increase between 1974 and 1982.

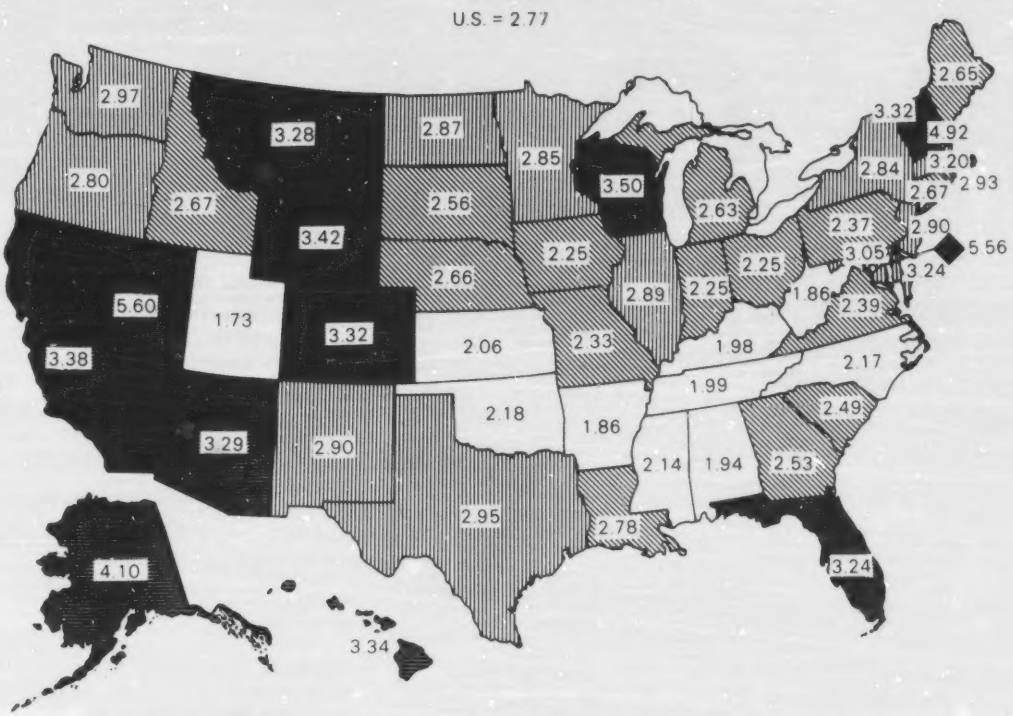
The survey data suggest that a substantial proportion of all alcohol is consumed by a relatively small fraction of the total drinking population (see figure 4). This figure shows that 50 percent of the alcohol is consumed by 10 percent of the population.

Surveys of Alcohol Consumption Among Youth and Young Adults

NIAAA has also sponsored a number of national surveys to assess alcohol consumption patterns and trends among the youth and young adult population. Two NIAAA surveys in 1974 and 1978 (Rachal et al. 1975, 1980) were followed in 1980 by the NIAAA-sponsored Gallup Youth Survey. In addition, the National Institute on Drug Abuse (NIDA) sponsors an annual survey of high school seniors and a biennial household survey (NIDA 1983a) that collects data on alcohol consumption of the youth population. These surveys showed a small decrease in the drinking levels among 16- to 18-year-olds for the years 1974, 1978, and 1980 (Zucker and Harford in press). The NIAAA data reveal some increase in the number of abstainers and a slight decrease in the proportion of moderate and heavy drinkers between the years 1978 and 1980.

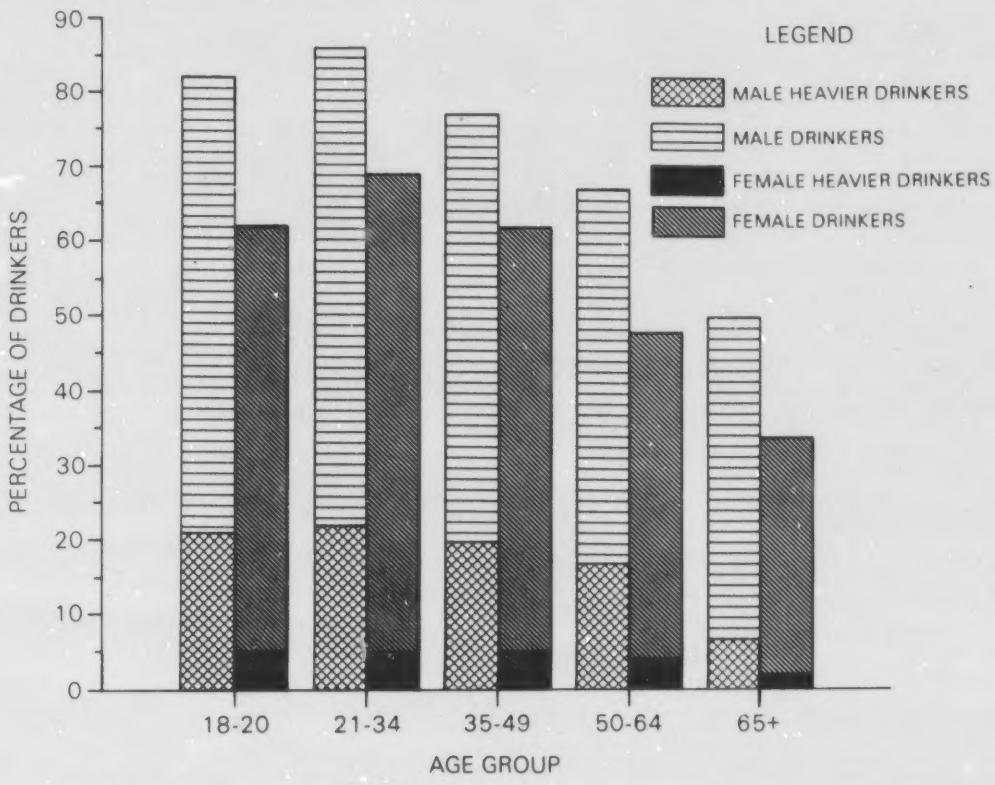
Similar conclusions can be drawn from the national surveys of high school seniors sponsored by NIDA since 1975 (NIDA 1983b). In a sample of approximately 130 public and pri-

Figure 2. Apparent Consumption of Ethanol from All Alcoholic Beverages in U.S. Gallons Per Capita of the Population Age 14 and Older, 1981



SOURCE: NIAAA 1982a,d,e.

Figure 3. Percentage of Drinkers by Age Group and Sex Averaged for the Period 1971-1976



SOURCE: Data from Clark, W.B. and Midanik, L. Alcohol Use and Alcohol Problems Among U.S. Adults: Results of the 1979 National Survey. Alcohol and Health Monograph No. 1. NIAAA, 1982. DHHS Publication No. (ADM) 82-1190

vate high schools selected to produce national estimates of drug-taking behavior among high school seniors, alcohol consumption among high school seniors has remained relatively stable from 1975 through 1982. The data on specific consumption show that more than 90 percent of surveyed seniors reported having used alcohol at least once during their lifetimes, and almost 90 percent reported using it in the past year. Six percent reported daily or nearly daily use during the month prior to the survey, and a significantly greater percentage reported occasional heavy drinking. Approximately 41 percent of the 1982 sample of high school seniors stated that, on at least one occasion during the 2-week period prior to the survey, they drank five or more drinks.

In general, young males report more drinking episodes and more daily use than females, and consumption of larger quantities of alcohol on a single drinking occasion. High school seniors from the South and the West apparently consume less alcohol than do those from the Northeast and the North Central regions.

These surveys of high school seniors also identified the grade at which an alcoholic beverage is first consumed. Approximately 10 percent of those surveyed had their first drink by the 6th grade. About 30 percent began drinking by the 8th grade, about 56 percent by the 9th grade, and about 75 percent by the 10th grade. By senior year (12th grade), fully 93 percent of those surveyed had had a drink. The surveys show very little change in this

pattern over time.

The surveys collected attitudinal information about alcohol consumption. In the 1981 survey, 22 percent believed consumption of one or two drinks daily to be harmful; 36 percent saw significant risk in having five or more daily drinks once or twice each weekend; and 65 percent believed that consumption of four or five drinks daily would result in significant harm. Thirty-one percent of the 1981 high school seniors did not disapprove of taking one or two drinks nearly every day. Little variation in these attitudes occurs over the 1975-1981 period (NIDA 1983a).

Finally, the NIDA survey data show a steady decline (except for the year 1979) in the 12- to 17-year-olds who reported taking a drink in the 30-day period prior to the survey. The drop from 37 percent in 1979 to 26 percent in 1982 may reflect recent changes in the legal age for purchasing alcohol in the majority of States. Future monitoring of the trends in alcohol consumption among teenagers and young adults will clarify these findings.

More detailed results of the NIDA surveys are summarized in Alcohol and Health Monograph No. 1 (Rachal et al. 1982).

Surveys of Alcohol Consumption During Pregnancy

Recently, national surveys have been conducted of a sample of married women who gave birth to live infants in 1980, as well as a sample of married women whose pregnancies terminated in a reported fetal death. These two surveys conducted by the National Center for Health Statistics (NCHS) collected information from married mothers, hospitals, physicians, and the birth or death certificates (Prager et al. in press). Data were collected on prenatal care, previous pregnancies, diagnostic and other procedures performed during pregnancy, and drinking and smoking behavior before and during pregnancy. (Additional data and discussion are included in the chapter on alcohol and pregnancy outcome.)

Preliminary analysis of 4,405 mothers giving live births show that women substantially reduce their alcohol consumption after they become pregnant (table 1). While 45 percent of these women abstained from alcohol use before pregnancy, approximately 61 percent abstained during pregnancy. The percentage of all mothers who were moderate/heavy drinkers (Level 2) declined from 12 percent before pregnancy to 2 percent during pregnancy.

Table 1 also shows changes in drinking from before pregnancy to during pregnancy. Of the 516 women who drank 0.25 ounces or more of absolute alcohol per day (Level 2) before pregnancy, only 16 percent continued to consume that amount during pregnancy, while 67 percent consumed less than that amount (Level 1), and 17 percent stopped drinking altogether. Similarly, of the 1,908 light drinkers (Level 1), 66 percent remained light drinkers,

Table 1. Number and percentage distribution of change in drinking behavior from before to during pregnancy, 1980

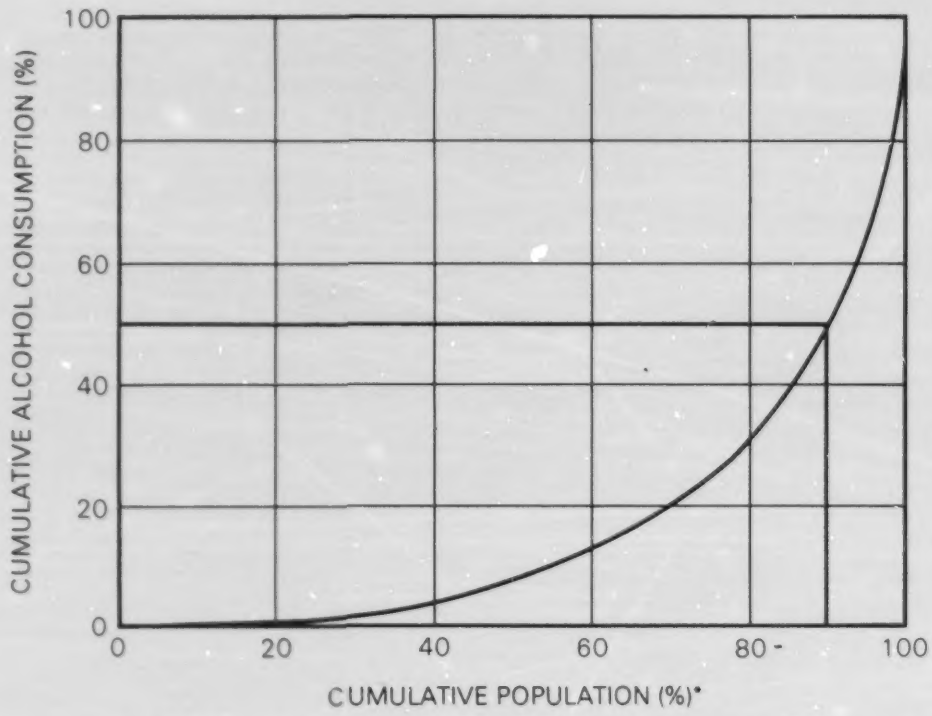
(Married mothers giving live births)

	Before pregnancy		During pregnancy		
	Number	Percent	Nondrinker	Level 1	Level 2
Nondrinker	1,981	45	99	1	1
Level 1	1,908	43	33	66	1
Level 2	516	12	17	67	16
Total	4,405	100	61	37	2

NOTE: Nondrinkers consumed less than one drink less than once a month. Level 1 drinkers consumed less than 0.25 ounces of absolute alcohol per day on the average. Level 2 drinkers consumed 0.25 or more ounces per day.

Source: Prager et al. in press.

Figure 4. Cumulative Distribution of Alcohol Consumption



*Drinkers only, aggregated from several U.S. national surveys, 1971-1975

SOURCE: AEDS data from HANES I Medical History Questionnaire and Louis Harris and Associates Surveys for 1972-1974

while 33 percent stopped drinking. These data confirm other research showing similar decreases (Little et al. 1976; Rosett et al. 1983).

This research also describes drinking behavior before and during pregnancy for several sociodemographic characteristics of married mothers giving live births. Black mothers drink less before and during pregnancy than white mothers. Hispanic mothers drink less than non-Hispanic mothers. Women with less education and from families with lower incomes drink less than women with more education or higher family incomes.

Alcohol-Related Mortality Attributed to Alcoholism, Alcoholic Psychosis, and Liver Cirrhosis

Three important causes of death attributed to excessive alcohol consumption are alcoholism, alcoholic psychosis, and cirrhosis of the liver. By definition, all deaths from alcoholism and alcoholic psychosis are alcohol related; however, alcohol is not the exclusive cause of cirrhosis of the liver. The 1979 U.S. mortality rate for alcoholism was 1.8 per

BEST COPY AVAILABLE

100,000 population, or approximately 4,000 deaths. The mortality rate in 1979 for alcoholic psychosis was 0.2 per 100,000 population, or about 440 deaths. Cirrhosis of the liver, the eighth leading cause of death in the United States in 1979, accounted for about 29,000 deaths, or 13.2 deaths per 100,000 population.

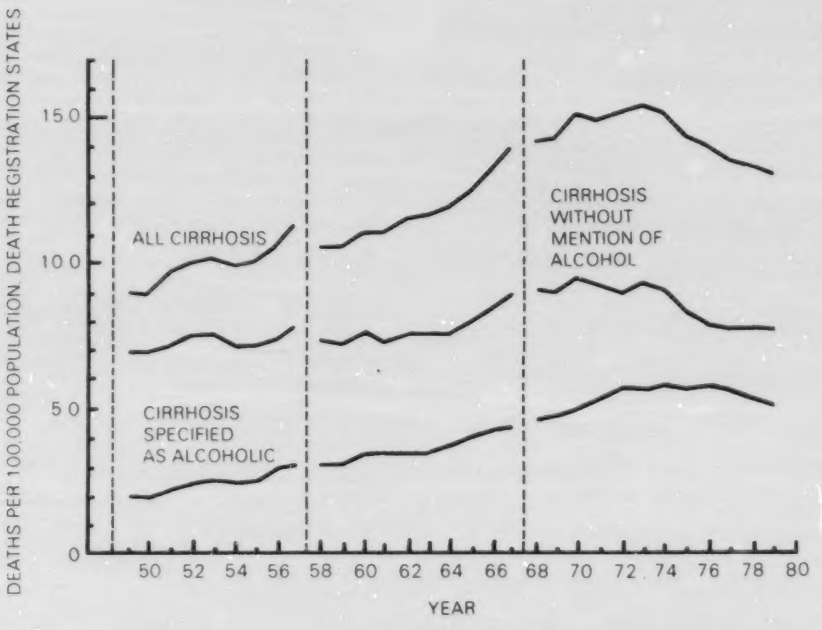
Since 1949, the death rates attributed to alcoholic psychosis and alcoholism have remained relatively stable, while the death rate attributed to cirrhosis of the liver rose until about 1973 and then began to decline (see figure 5). The U.S. mortality rate for cirrhosis decreased 12 percent between 1973 and 1979. The overall decline in the cirrhosis death rate appears to be due to factors other than alcohol; alcohol-related cirrhosis death rates have remained stable at approximately 5 deaths per 100,000 population (Malin et al. 1982a).

Alcohol-Related Causes of Hospitalization[1]

The national vital statistics record system of the National Center for Health Statistics (NCHS) collects and tabulates mortality information by cause of death for the entire U.S. population, but no comparable data system exists to collect and tabulate statistics on morbidity (disease) for the entire population. The Hospital Discharge Survey (HDS) operated by NCHS approximates a national morbidity surveillance system by sampling more than 225,000 records from over 400 participating hospitals on an annual basis.

[1] This section summarizes various reports prepared by the National Center for Health Statistics. These reports have been cumulated in the references.

Figure 5. Trends in Cirrhosis Mortality Rates With and Without Mention of Alcohol in the United States, 1949-1979



SOURCE: Malin (1982) and personal communication with Mortality Branch, National Center for Health Statistics

BEST COPY AVAILABLE

National estimates have been made for the years 1971 through 1980 on the numbers and rates of patients discharged with diagnoses of alcoholism, alcoholic psychosis, and cirrhosis of the liver. Because of sampling variability in the HDS from year to year and the relatively low frequency of some diagnoses, monitoring trends over time must be viewed with caution. Nonetheless, the data suggest a significant increase in the number of persons hospitalized for alcoholism during the 1970s. For example, there were an estimated 200,000 alcoholism discharges in 1971 compared with an estimate of 519,000 alcoholism discharges in 1978, an increase of more than 160 percent. During this same period, the national mortality rates remained relatively stable.

When HDS data are considered by sex, the rates for discharges with alcoholism are 3-1/2 to 4-1/2 times greater for males than for females. While the numbers and rates of discharges with alcoholism have increased for both sexes, this ratio has remained fairly constant. The male rate for hospital discharges for cirrhosis of the liver has remained stable through the 1970s at about 1-1/2 times the female rate.

Alcohol-Related Problems in Veterans

Data from the Veterans Administration (VA 1982) show that a substantial fraction of the nearly 1 million discharges from VA hospitals in 1980 had an alcohol-related disorder, including alcoholic psychosis, alcoholism, organic brain syndrome, and alcoholic cirrhosis of the liver. Such disorders constitute the second largest category of diagnoses (next to heart disease) among patients discharged from VA hospitals. The proportion rose from 15 percent in 1970 to 19 percent in 1974 and 1975 and has dropped slightly to 17 percent in 1977-1980. Nearly two-thirds of these discharges had a principal diagnosis that was alcohol related.

Periodically, the VA conducts a census of hospitalized patients (VA 1982). During the 1970s, the rate of patient hospitalizations with an alcohol-related principal diagnosis was relatively stable at about 8 to 10 percent each year. In some years, the VA has also estimated the number of problem drinkers, who constitute an additional 5 to 6 percent of the patient census. When problem drinkers are added to those patients identified as alcoholic, about 25 percent of the entire VA patient load have alcohol-related problems that contribute to their medical disabilities.

Since 1970, the proportion of VA patients with alcoholism or problem drinking has more than doubled for those under age 35 (15 percent to 35 percent). This marked increase reflects the growth in alcohol-related disabilities from the Vietnam era. The reasons for this substantial increase remain to be identified. It is not clear whether (a) this increase is specific to the VA beneficiary program, (b) the statistics reflect a more general increase among all men of comparable age, (c) younger veterans have a greater proportion of alcohol problems simply because the incidence of other health conditions such as cancer or stroke is less in this population, or (d) the increases are attributable to some combination of these and other reasons. The trend over time does reflect, in part, the aging of this group, increased years of drinking, and a greater probability of being diagnosed as alcoholic. In response to alcohol problems, the VA has promoted specialized alcohol dependence treatment programs, which have multiplied from 8 in 1970 to 100 in 1980.

Alcohol-Related Problems Among Native Americans

Alcohol-related mortality is a major problem among Native Americans, with cirrhosis of the liver the fourth leading cause of death. Accidents are the leading cause, and the contribution of alcohol to fatal mishaps is substantial. Death rates attributable to major alcohol-related causes of death (alcoholism, alcoholic psychosis, and cirrhosis of the liver with mention of alcoholism) are about eight times greater among Native Americans than for the U.S. population as a whole (Indian Health Service 1982a).

Hospital discharge rates from the Indian Health Services (IHS) hospital system for alcohol-related diagnoses are about three times the rates for the entire United States and double the rates for races other than white. This higher IHS alcohol-related discharge rate applies to both males and females. For ages 15 to 44 years, generally years of high productivity, the IHS hospital discharge rate for alcohol-related diagnoses is more than four times that of the rate for the total United States (Indian Health Service 1982b).

Table 2 shows age-specific hospital discharge rates for the IHS and for the United States as a whole in 1981. IHS discharges are from IHS and general hospitals under contract to the IHS, while U.S. discharges are from

non-Federal short-stay hospitals. The alcoholic psychosis rate for all ages for IHS discharges is four times as great (11.8 vs. 2.9 per 100,000) as the discharge rate for the United States as a whole. The discharge rates for nondependent abuse of alcohol and for alcoholic liver disease are 3.4 times as great (5.8 versus 1.7 and 6.4 versus 1.9, respectively), and the alcohol dependence syndrome rate is nearly double that for the total United States (35.8 versus 19.7). The table also shows these comparisons for specific age groups where the differences are even greater.

Alcohol-Related Motor Vehicle Fatalities

Motor vehicle accidents have claimed between 45,000 and 55,000 lives annually over the past decade. While the death rate per 100 million vehicle miles has in general declined by more than 25 percent (perhaps as the result of the post-oil-embargo lower speed limit and more rigorous enforcement), motor vehicle crashes have become one of the Nation's leading causes of death for all age groups and the leading cause of death for persons aged 15 to 24 years. In this age group, motor vehicle fatalities account for about 40 percent of all deaths.

The National Highway Traffic Safety Administration (NHTSA) maintains national surveillance of all traffic crashes involving one or more fatalities, the Fatal Accident Reporting System (FARS). For every fatal accident, FARS provides data on each vehicle, each driver, and each person involved in the accident, including a subjective characterization of alcohol involvement when it is known. In 1981, the blood alcohol concentration (BAC) was known for only 30 percent of the 62,120 drivers involved in fatal traffic crashes (see table 3). Among these 18,540 drivers, 6,349 (34 percent) had no detectable BAC at the time of the testing; 2,450 (13 percent) had BACs between 0.01 and 0.09 percent; while the remaining 9,741 (53 percent) had BACs of 0.10 percent or higher, the level of legal intoxication in all but three States. In addition, of the 48,069 deaths that occurred in 1981, 20,658 (43 percent) were known to involve alcohol.

Alcohol involvement in accidents is especially common in single-vehicle crashes, in which young people are disproportionately involved (see table 4). The 16- to 24-year-old age group accounts for only 16.5 percent of the U.S. population but 41 percent of the single-vehicle accident fatalities and 45 percent of all single-vehicle fatal accidents involving alcohol. In contrast, the 55-and-older age group represents 21 percent of the population but accounts for only 11 percent of all single-vehicle accident fatalities and 5.5 percent of the single-vehicle accidents involving

Table 2. Discharge rates per 10,000 from Indian Health Service and contract general hospitals and from non-Federal short-stay hospitals by first-listed diagnosis and age, 1981

Age at admission	Alcoholic psychosis		Alcoholic dependence syndrome		Alcoholic nondependent abuse of alcohol		Liver disease	
	IHS rate	U.S. rate	IHS rate	U.S. rate	IHS rate	U.S. rate	IHS rate	U.S. rate
All ages	11.8	2.9	35.8	19.7	5.8	1.7	6.4	1.9
Under 15 years	0.0	0.0	0.6	0.6	0.9	0.4	0.0	0.0
15-44 years	19.0	3.1	50.5	22.6	8.6	2.1	8.0	1.1
45-64 years	20.1	6.3	83.2	38.3	8.9	2.3	18.9	5.2
65 years and over	4.9	2.0	21.7	13.6	4.4	1.6	4.2	2.4

Source: Indian Health Service 1982b.

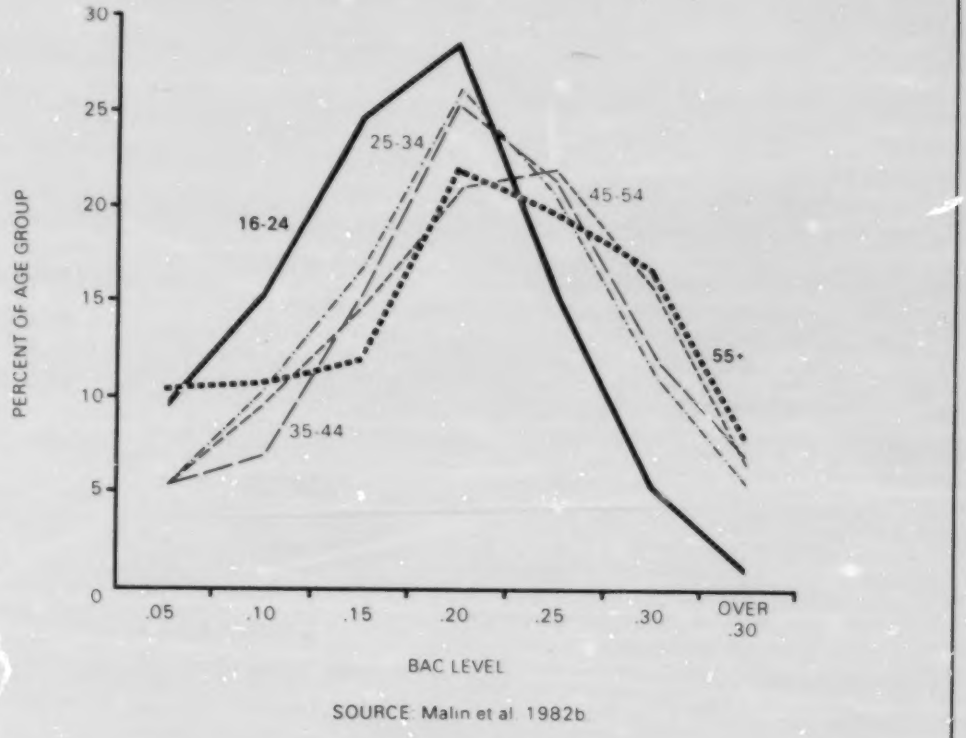
Table 3. Alcohol involvement by performance measure and by alcohol test results (BAC) of drivers in fatal traffic accidents, 1981

Alcohol involvement determined by performance measure[a]	Alcohol test results (BAC) 0	.01-.09	.10 and +	Persons tested Number	Percent	Drivers in fatal accidents
No	6,136	2	2	6,140	14	42,878
Yes	213	2,448	9,739	12,400	64	19,242
Total	6,349	2,450	9,741	18,540	30	62,120

[a] When suspected of drinking by an investigating officer, a driver's poor response to performance measures, such as the ability to walk a straight line, generally leads to a label of "alcohol involvement" on the investigative report.

Source: NIAAA 1983.

Figure 6. Percentage of Drivers With Positive Blood Alcohol Concentration (BAC) by Age Group in Single Vehicle Accidents, 1981



SOURCE: Malin et al. 1982b

alcohol. Young drivers are even more disproportionately involved in single-vehicle accidents when other factors such as average miles driven and proportion licensed to drive are considered. Fewer young drivers are licensed than their older counterparts and they drive less on average.

Figure 6 shows the percentage of drivers in single-vehicle fatal accidents in each age group at various levels of BAC. Greater percentages of young drivers have lower BACs than older drivers. This suggests that younger drivers become involved in fatal accidents at lower BAC levels than older drivers (Malin et al. 1982b).

Drivers involved in alcohol-related fatal crashes have a higher frequency of previously recorded accidents, license suspensions and revocations, and convictions for driving while intoxicated (DWI), as well as a higher proportion of previously recorded speeding convictions and "other harmful moving violations." For the 62,120 drivers involved (but not necessarily killed themselves) in fatal traffic crashes in 1981, data were collected on their previous convictions for DWI. Among the drivers who were tested and found to have no detectable BAC, 2 percent had a previous DWI conviction. Among the drivers whose BAC was in the range from 0.01 to 0.09 percent, 5 percent had a previous DWI conviction. Among the drivers with BACs of 0.10 or greater, 11 percent had previous DWI convictions, a rate 5.5 times greater than the group without detectable BAC (NIAAA 1983).

Alcohol- and non-alcohol-related traffic fatalities appear to follow similar monthly variations. For both groups, fatalities are higher in summer months when more vehicle miles are driven, while in winter they tend to fall below the average monthly rate.

Figure 7 displays the day of week and the time of day for all fatalities in 1981. Fatalities in accidents with no known alcohol involvement peaked between 4 p.m. and 8 p.m. on Sunday through Thursday. In contrast, the alcohol-related fatalities peaked later in the evening (8 p.m. to 4 a.m.) for Monday through Thursday. Similarly, on Friday and Saturday, the greatest number of non-alcohol-related fatalities occurred between 4 p.m. and 4 a.m., while alcohol-related fatalities occurred later (midnight to 4 a.m.) and were much higher than the weekend maximums for fatalities with no known alcohol involvement (NIAAA 1983).

Summary

In summary, it can be said that the acquisition of new knowledge about the epidemiologic factors affecting alcohol abuse and alcoholism is increasing. Advances in knowledge have been hampered by a lack of uniformly applied definitions of terms such as alcoholism and alcohol abuse, but there are encouraging signs of progress.

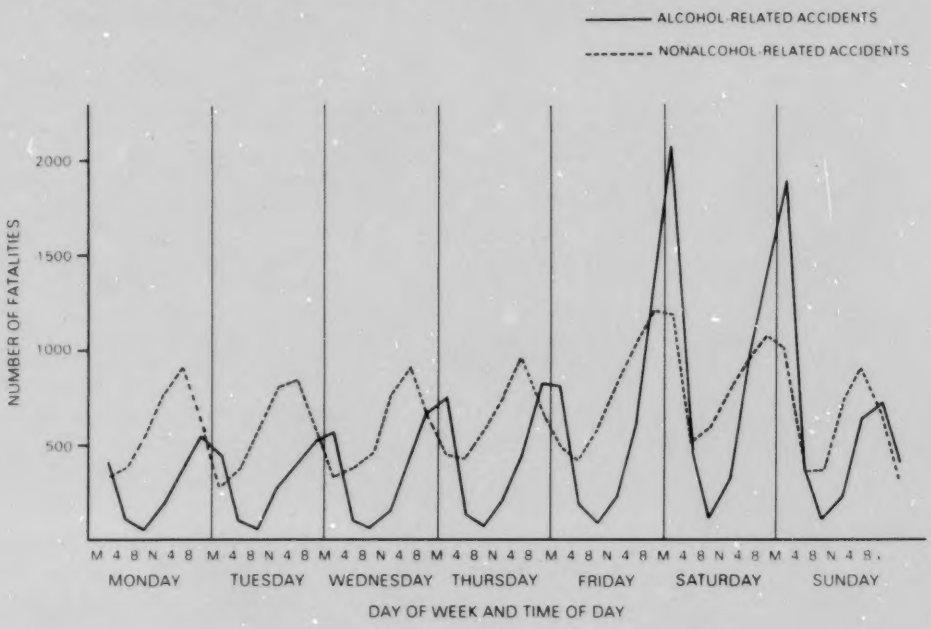
The per capita alcohol consumption continues to rise, although not as steeply as in

Table 4. Fatal single-vehicle accidents by age of driver and alcohol involvement, 1981

Age group	U.S. population (percent)	Number single-vehicle accidents	Total (percent)	Number accidents with alcohol	Alcohol-involved accidents (percent)
16-24	16.5	10,295	41.0	3,190	44.6
25-34	16.8	6,977	27.8	2,193	30.6
35-44	11.5	3,165	12.6	902	12.6
45-54	9.9	2,002	8.0	476	6.6
55+	21.1	2,656	10.6	397	5.5
Totals		25,095	100.0	7,158	100.0

Source: Malin et al. 1982b.

Figure 7. Number of Fatalities by Day of Week, Time of Day, and Alcohol Involvement, 1981


ALCOHOL-RELATED ACCIDENTS
NONALCOHOL-RELATED ACCIDENTS
NUMBER OF FATALITIES
2000
1500
1000
500
M 4 8 N 4 8 M 4 8 N 4 8 M 4 8 N 4 8 M 4 8 N 4 8 M 4 8 N 4 8 M 4 8 N 4 8 M 4 8 N 4 8.
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
SATURDAY
SUNDAY
DAY OF WEEK AND TIME OF DAY

SOURCE AEDS data from NHTSA Fatal Accident Reporting System (FARS) for 1981

earlier decades. About a third of the total population abstains from alcohol consumption during the typical year, another third consumes an average of less than one drink every other day, while the remaining third drinks more heavily.

Women substantially reduce their alcohol consumption after they become pregnant. While 45 percent abstain before pregnancy, 61 percent are abstainers during their pregnancy period. Similarly, 12 percent are moderate to heavy drinkers before pregnancy, while only 2 percent continue drinking to this extent after they become pregnant.

Overall mortality from major alcohol-related causes of death has remained relatively stable. Alcohol-related disease appears to have fallen from a high point in 1973, but liver cirrhosis has decreased only slightly.

Within the Veterans Administration hospital system, alcohol-related disorders have dropped from previous high levels in the 1970s. However, the proportion of veterans under age 35 with alcohol-related problems has increased substantially. Alcohol-related problems among Native Americans continue to be a major source of both morbidity (disease) and mortality, with alcohol-related disorders among Native Americans being several times higher than for the U.S. population as a whole.

A substantial fraction of the Nation's traffic fatalities continues to be associated with alcohol consumption. More than half the drivers involved in fatal accidents are intoxicated. Drinking drivers involved in fatal crashes tend to have poorer driving records, including a higher frequency of previously recorded accidents, a higher frequency of previously recorded license suspensions and/or revocations, and a higher proportion of previously recorded speeding convictions than nondrinking drivers in similar accidents.

Epidemiological research continues to clarify the nature and extent of alcohol abuse and alcoholism. Increased knowledge and application of that knowledge to prevention and treatment could help reduce the individual and social costs of alcohol abuse and alcoholism.

References

Clark, W.B., and Midanik, L. Alcohol use and alcohol problems among U.S. adults. Results of the 1979 national survey. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM) 82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 3-52.

Indian Health Service. Analysis of Fiscal Year 1981 IHS and U.S. Hospital Discharge Rates by Age and Primary Diagnosis. Rockville, Md.: IHS, August 1982a.

Indian Health Service. "Chart Series" Tables. FY 1983 ed. Rockville, Md.: IHS, Office of Program Statistics, March 1982b.

Little, R.E.; Schultz, F.A.; and Mandell, W. Drinking during pregnancy. Journal of Studies on Alcohol 37:375-379, 1976.

Malin, H.; Coakley, J.; Kaelber, C.; Munch, N.; and Holland, W. An epidemiologic perspective on alcohol use and abuse in the United States. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM) 82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982a. pp. 99-153.

Malin, H.J.; Trumble, J.; Kaelber, C.T.; and Lubran, B. Alcohol-related highway fatalities among young drivers--United States. Morbidity and Mortality Weekly Report 31 (48):641-644, 1982b.

National Center for Health Statistics. Detailed diagnoses and surgical procedures for patients discharged from short-stay hospitals: United States, 1977, DHHS Pub. No. (PHS) 79-1274; 1977, DHHS Pub. No. (PHS) 80-1274. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1979, 1980.

National Center for Health Statistics. Inpatient utilization of short-stay hospitals by diagnosis: United States, 1971. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 16. DHEW Pub. No. (HRA) 75-1767; 1972. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 20 DHEW Pub. No. (HRA) 76-1771; 1973. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 25 DHEW Pub. No. (HRA) 77-1776; 1974. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 30 DHEW Pub. No. (HRA) 77-1785; 1978. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 55 DHHS Pub. No. (PHS) 81-1716. Hyattsville, Md.: NCHS, 1974, 1975, 1976, 1977, 1981.

National Center for Health Statistics. Standardized microdata tape transcript. 1975 Hospital Discharge Survey. Hyattsville, Md.: NCHS, n.d. NTIS No. PB-270-773; 1976 Hospital Discharge Survey. Hyattsville, Md.: NCHS, n.d. NTIS Order No. PB-82-179-227.

National Center for Health Statistics. Utilization of short-stay hospitals: Annual summary for the United States, 1979. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 60. DHHS Pub. No. (PHS) 82-1721; 1980. Vital and Health Statistics, Series 13: Data from the National Health Survey, No. 64 DHHS Pub. No. (PHS) 82-1725. Hyattsville, Md.: NCHS, 1981, 1982.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. Analysis of Data From FARS for the Year 1981. Rockville, Md.: NIAAA, April 1983.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. U.S. Apparent Consumption of Alcoholic Beverages Based on State Sales, Taxation, or Receipt Data. U.S. Alcohol Epidemiologic Data Reference Manual, Section 1. Rockville, Md.: NIAAA, 1982a. NTIS No. PB-82-187-113.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. Cirrhosis of Liver Mortality in the United States, Each State and County and Selected SMSAs. U.S. Alcohol Epidemiologic Data Reference Manual, Section 2. Rockville, Md.: NIAAA, 1982b. NTIS No. PB-82-187-097.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. Hospital Discharges With Alcohol-Related Conditions. Hospital Discharge Survey, 1975-1977. U.S. Alcohol Epidemiologic Data Reference Manual, Section 4. Rockville, Md.: NIAAA, 1982c. NTIS No. PB-82-187-121.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. U.S. Apparent Consumption for Calendar Year 1980. AEDS Working Paper #50. Rockville, Md.: NIAAA, June 1982d.

National Institute on Alcohol Abuse and Alcoholism, Alcohol Epidemiologic Data System. U.S. Apparent Consumption for Calendar Year 1981. AEDS Working Paper #55. Rockville, Md.: NIAAA, June 1982e.

National Institute on Drug Abuse. National household survey on drug abuse. NIDA Capsules C83-1:1-3, February 1983a.

National Institute on Drug Abuse. Student Drug Abuse in America, 1975-1982. DHHS Pub. No. (ADM) 83-1260. Rockville, Md.: NIDA, 1983b.

Prager, W.; Malin, H.; Graves, C.; Spiegler, D.; Richards, L.; and Placek, P. "Smoking and Drinking Behavior Before and During Pregnancy of Mothers of Live-born Infants." U.S. Department of Health and Human Services. National Center for Health Statistics, Health U.S. 83, in press.

Rachal, J.V.; Guess, L.L.; Hubbard, R.L.; Maisto, S.A.; Cavanaugh, E.R.; Waddell, R.; and Benrud, C.H. Adolescent Drinking Behavior *M-1978, Vol. 1. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1980.

Rachal, J.V.; Maisto, S.A.; Guess, L.L.; and Hubbard, R.L. Alcohol use among youth. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM) 82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 55-93.

Rachal, J.V.; Williams, J.R.; Brehm, M.L.; Cavanaugh, B.; Moore, R.P.; and Eckerman, W.C. A National Study of Adolescent Drinking Behavior, Attitudes and Correlates. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1975. NTIS No. PB-246-002.

Rosett, H.L.; Weiner, L.; Lee, A.; Zuckerman, B.; Dooling, E.; and Oppenheimer, E. Patterns of alcohol consumption and fetal development. Obstetrics and Gynecology 61 (5):539-546, 1983.

U.S. Department of Health, Education, and Welfare. Third Special Report to the U.S. Congress on Alcohol and Health. Noble, E.P., ed. DHEW Pub. No. (ADM) 79-832. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1978.

Veterans Administration. Office of Reports and Statistics. Alcoholism and Problem Drinking, 1970-1975: A Statistical Analysis of VA Hospital Patients. 1980 Supp. Biometrics Monograph No. 14. Washington, D.C.: VA, 1982.

Zucker, R.A., and Harford, T.O. A national study of adolescent drinking practices in 1980. Journal of Studies on Alcohol, in press.

Chapter II

Genetics and Alcoholism

One of the most keenly debated issues in alcoholism research has been whether genetic factors play an important part in the development of alcoholism. In other words, is susceptibility to alcoholism inherited, at least in some individuals? If so, what are the predisposing factors? To what extent do environmental influences determine the expression and severity of the disorder?

An affirmative answer to the first question began to emerge 10 years ago with the Goodwin et al. (1973) study on adopted-out sons of alcoholics, although the results were initially greeted with skepticism. Impressive evidence now indicates that heritable factors influence susceptibility to alcoholism as well as to a number of physiological and biochemical responses to alcohol consumption. Furthermore, research has documented that environmental and hereditary factors interact to produce the alcoholic state in some individuals.

Heritability of Alcoholism—Early Studies

The notion that alcoholism runs in families dates back centuries. Reports before 1900 on the familial nature of alcoholism were primarily anecdotal. In the past 80 years, however, more than 100 studies have examined the familial incidence of alcoholism (Goodwin 1971). In reviewing 39 studies conducted over the past four decades, Cotton (1979) summarized statistics on the families of 6,251 alcoholics and 4,083 nonalcoholics. The most striking finding was that, regardless of the nature of the nonalcoholic comparison population, alcoholics were more likely than nonalcoholics to have an alcoholic father, mother, sibling, or distant relative. On the average, almost one-third of any sample of alcoholics had at least one parent with an alcoholism problem. Alcoholic patients were six times more likely than nonpsychiatric patients and two times more likely than psychiatric patients to report parental alcoholism. Thus, the high rate of parental alcoholism appeared to be not a general characteristic of a disturbed population but a specific correlate of alcoholism. Alcoholism was more prevalent in male relatives, in the families of female alcoholics, and in near relatives than in distant relatives.

The results of family studies do not unequivocally support genetic transmission. A family shares a common environment as well as common genes, and familial patterns of alcoholism can be explained just as readily by behavioral and sociocultural theories as by genetic ones. Although evidence in support of environmental theories is tenuous, such factors cannot be ignored. It is notable that, in the family studies summarized by Cotton (1979), 45 to 80 percent of the alcoholic subjects did not have an alcoholic parent or other relative. This suggests that in many individuals environmental factors influence the expression and severity of the disorder.

To separate the influence of heredity from that of environment, studies are needed comparing special populations in which the influence of either heredity or environment differs (e.g., comparing rates of alcoholism among identical versus fraternal twins or between half-siblings, or comparing such rates among adopted children of alcoholics versus those who are raised by their biological parents). All of these special population groups have been used in alcohol-related research. A number of studies have compared identical and fraternal twins with regard to alcohol-drinking practices, alcohol metabolism, and the effect of alcohol on brain waves as measured by electroencephalogram (EEG). None specifically investigated clinically defined alcoholism, however.

In 1972, Schuckit and coworkers reported on a study of alcoholism in half-siblings. The 69 probands (alcoholic subjects who brought their families into the study) were hospitalized patients who had half-siblings and had been diagnosed as having primary alcoholism, i.e.,

alcohol abuse without preexisting psychiatric disorder. Thirty-two of the 164 half-siblings were alcoholic. It was found that 62 percent of the alcoholic but only 20 percent of the nonalcoholic half-siblings had at least one alcoholic biological parent. This difference was statistically highly significant. Further, the alcoholic half-siblings had not lived in an alcoholic environment any more frequently than had the nonalcoholic half-siblings. Half-siblings who shared the childhood environment of the alcoholic proband did not have an increased rate of alcoholism. These results suggested that genetic predisposition was more important than childhood environment in influencing the development of alcoholism.

A cleaner separation of genetic and environmental factors can be achieved by studying subjects who were adopted or placed in foster homes at an early age. Such an approach was first employed by Roe (1944), but the study was flawed by its small sample size and by uncertainty about the validity of the diagnostic criteria used to indicate alcoholism.

The study by Goodwin and associates (1973) of adopted sons of alcoholics in Denmark drew from a larger sample population, 5,483 non-blood-related adoption cases, and used a stringent set of criteria for diagnosing alcoholism. The probands were 55 adopted-out sons of alcoholics and the control group consisted of 78 adopted-out sons of nonalcoholics, matched to the probands by current age and age at adoption. Alcoholism was defined as heavy drinking leading to problems in at least three of four areas, two social and two medical and physiological. Sons of alcoholics were found to be more than three times as likely to become alconolic as were sons of nonalcoholics. They were also more likely to be alcoholic at a relatively early age and to have a form of alcoholism sufficiently serious to warrant treatment. Sons of alcoholics were shown as no more likely to be heavy drinkers than were sons of nonalcoholics, and having an alcoholic biological parent did not appear to predispose individuals to psychiatric disorders.

Some of the probands had brothers who had been raised by their alcoholic biological parent. A second phase of the Danish adoption studies compared the rate of alcoholism in these adopted and nonadopted siblings (Goodwin et al. 1974). Nonadopted siblings were no more frequently alcoholic than were their adopted-out brothers who were raised in a nonalcoholic environment. The investigators therefore concluded that exposure to an alcoholic family environment did not increase the potential for alcoholism in genetically susceptible individuals. Adopted-out daughters of alcoholics and of nonalcoholics were also compared (Goodwin et al. 1977), but because so few alcoholics were found in either group, no conclusion could be drawn regarding genetic predisposition in women.

Heritability of Alcoholism—Recent Studies

Confirmation of the findings of Goodwin and coworkers came quickly from researchers in Sweden and the United States. Bohman (1978) compared the rates of alcohol abuse in 2,324 adoptees (1,125 men and 1,199 women) and in their biological parents (2,261 mothers and 1,902 fathers of established paternity). The adoptees had been born in the Stockholm area between 1930 and 1949 and had been placed in adoptive homes before the age of 3. Histories of alcohol abuse were sought in the records of the excise board, the health insurance office, and other public agencies. The excise board's register contained information on fines imposed for intemperance, treatment for alcoholism, and supervision of chronically alcoholic persons. (Scandinavian countries are ideally suited for large studies of this sort, owing to their systems of public recordkeeping and the accessibility of these records for research use.)

The Bohman study showed that adopted sons whose biological fathers were alcoholic were three times as likely to become alcoholic as were the adopted sons of nonalcoholic fathers. Adopted sons whose biological mothers were alcoholic were twice as likely to become alcoholic as were the adopted sons of nonalcoholic mothers. Registration rates for alcohol abuse were the same among adopted women, regardless of their biological parents' records of alcohol abuse. The findings suggested that genetic factors influenced the occurrence of alcohol abuse in men, but the study's small sample size precluded a judgment about women.

Some of the data were also analyzed in the manner of a control study, comparable to that employed by Goodwin and coworkers (1973). From the 2,324 adoptees, 192 probands whose parents had the most frequent or serious records of alcohol abuse were selected. These probands included 50 men and 50 women whose biological fathers had been reported for repeated and severe alcohol abuse and had been hospitalized for treatment of alcoholism. An

additional 42 men and 50 women whose biological mothers had been reported for alcohol abuse were included as well. The subjects were compared with four control groups selected from the same population on the basis of age, sex, age at adoption, occupational category of the adoptive parents, and ages of the biological and adoptive parents when the child was born.

Male adoptees whose fathers were reported as having severe alcoholism showed a 20 percent incidence of alcohol abuse compared with 6 percent in the controls. In the adopted men whose biological mothers had been reported for alcohol abuse, 33 percent were reported for alcohol abuse as compared with 19 percent in the control group--however, the difference is not statistically significant. On the whole, these findings again confirm the data of Goodwin and coworkers (1973) concerning a genetic influence on alcoholism or alcohol abuse in the sons of male alcoholics.

Adopted women whose biological parents were reported for alcohol abuse, as well as adopted women with non-alcohol-abusing biological parents, had low rates of alcohol abuse. Because of this outcome, a conclusion about the presence or lack of genetic influence on alcohol abuse in women could not be made.

Researchers at the University of Iowa (Cadoret and Gath 1978; Cadoret et al. 1980) have contributed two reports on alcoholism in American adoptees. The first study focused on male and female adoptees who had been separated at birth from biological parents who showed evidence of psychiatric or behavior disturbance. Biological parents of the control group adoptees were not mentally disturbed. The experimental and control groups were matched on age, sex, time spent in foster care, and age of biological mother at birth of her child. Data were collected on 84 of 173 adult adoptees by interview, either with the adoptive parents or with both adoptee and adoptive parents. The remainder of the identified adoptees (51 percent) either could not be located or refused to be interviewed.

Two or more social or medical complications of excessive alcohol use or hospitalization for detoxification constituted a diagnosis of alcoholism (Feighner et al. 1972). The alcoholism rate was low in both the experimental and control groups. Three adoptees with primary alcoholism were associated with 6 alcoholic biological parents versus 1 alcoholic adoptee from 78 biological parents without alcoholism. Seven adoptees had secondary alcoholism (alcoholism occurring with and preceded by adult psychiatric disorders), but none of them had alcoholic biological parents. Adoptee alcoholism was found to be unrelated to psychiatric diagnoses in biological parents or to a variety of psychosocial and environmental variables in postnatal life. It was, however, significantly correlated with childhood conduct disorders in the adoptees and with alcoholism and alcohol abuse in the biological parents.

In the second Iowa study, only male adoptees were studied, but the sample was enlarged to include adoptees whose second-degree relatives (e.g., grandparents, aunts, uncles, cousins) had psychiatric or behavior disturbances. A matched control group was also recruited. Out of the 167 male adoptees 18 years and older thus identified, data were collected on 92 men (55 percent) by interview with the adoptee, the adoptive parent, or both. The studies were marred by high dropout rates; as measured by available information on participants and nonparticipants, however, sample bias in the two studies was estimated to be minimal. Of the 92 male adoptees, 23 were alcoholic and 22 had experienced childhood conduct disorders. Evidence for alcoholism was present in 15 first and second-degree relatives. Statistically significant associations existed between adoptee alcoholism and an alcoholic family (biological) background and between childhood disorder and the development of alcoholism in adulthood. None of the environmental factors, including psychiatric or alcohol problems in the adoptive family as well as its socioeconomic status, predicted alcoholism.

Both studies confirm the conclusions of Goodwin and coworkers "that genetic factors importantly affect alcoholism development." But both failed to demonstrate an independent effect of environmental factors in the development of alcoholism. Also, the association of childhood conduct disorders with alcoholism in adult life is in accord with previous reports suggesting that childhood conduct disorder and hyperactivity may predict subsequent alcoholism (Schuckit et al. 1972; Goodwin et al. 1975).

Environmental-Genetic Influence on Alcoholism

The adoption studies described here clearly demonstrate that genetic predisposition is an

important determinant of alcoholism in some individuals. What then is the contribution of environmental influences to the expression of alcoholism in other individuals? Do these influences affect severity of the disorder in the genetically susceptible individual?

In other words, are subtypes of alcoholism and alcohol abuse each affected to different extents by genetic and environmental variables? To study these questions, researchers from Washington University in St. Louis and from Sweden collaborated to analyze further the population of adoptees studied by Bohman (1978). This research team first examined adopted men with alcohol abuse problems (Cloninger et al. 1981). Out of 1,125 adopted men in the Stockholm adoption study reported by Bohman, 862 subjects were selected whose paternity was known and who were adopted before the age of 3 by nonrelatives.

These adoptees were first divided into groups according to severity of alcohol abuse. Mild abuse was defined as one registration for abuse (by the excise board) without treatment. Moderate abusers had two or three registrations without treatment, whereas severe abusers had at least four registrations and compulsory treatment or psychiatric hospitalization for alcoholism. The characteristics of the biological parents (e.g., severity of alcohol abuse, occupational status) and of postnatal environment (e.g., occupational status of adoptive father, age at adoptive placement) were analyzed to find which factors would best distinguish one group from another. The discriminant characteristics of each group were then applied to the total population to measure the extent to which these characteristics contributed to the number of individuals with alcohol problems.

As a result of these statistical analyses, two heritable subtypes of alcoholism were identified, which the authors named Type I (or milieu-limited) and Type II (or male-limited). Type I alcohol abuse occurred in 13 percent of the adopted men. Both their biological fathers and mothers typically exhibited mild alcohol abuse requiring no treatment, and postnatal environment determined both the frequency and the severity of alcohol abuse in the susceptible sons. The sons' alcohol abuse was usually mild or isolated, but could be severe, depending upon the nature of the environmental provocation. With such provocation, the relative risk of developing alcohol abuse in congenitally predisposed individuals was increased twofold; without it, the risk was the same as that in the general population.

Type II alcohol abuse occurred in 4 percent of the adopted men. It represented, therefore, about 25 percent of the alcohol abusers in the study. Their biological fathers, but not their mothers, had severe alcoholism requiring extensive treatment. Postnatal environment had no effect on the expected numbers of abusers but may have influenced severity. Alcohol abuse in the susceptible sons was usually recurrent and moderate, although sometimes it was severe. An estimated ninefold increase in risk of developing alcohol abuse or alcoholism was evident in the affected individuals, regardless of postnatal environment. The characteristics of this type of alcohol abuse/alcoholism are similar to those described in the Danish adoption studies (Goodwin et al. 1973).

It is notable that an average of 60 percent of the men in all three categories of alcohol abuse had no family history of abuse. Their alcohol abuse may have been caused by other disorders, such as psychiatric or behavioral. Alternatively, they could represent, in part, a group whose parents were genetically susceptible to alcohol abuse but lacked the necessary environmental provocation to become abusers. This issue remains unresolved.

Bohman et al. (1981) studied adopted women, using a similar statistical analysis. From the 1,199 adoptees originally reported by Bohman (1978), 913 satisfied the entry criteria. Because only 31 women (3.3 percent) out of this sample were alcohol abusers, they were not grouped by severity of abuse. A fourfold increase in alcohol abuse occurred in the adopted women if their biological mothers were alcohol abusers. A relationship between alcohol abuse in the biological father and that in the daughter was less clear-cut. It appeared, therefore, that in daughters maternal alcohol abuse was a more significant predictor of abuse than was paternal alcohol abuse or alcoholism. Both biological parents of alcohol-abusing female adoptees were mild alcohol abusers who usually did not require extensive treatment. When young, the alcohol-abusing female adoptees were frequently placed in rural homes in which adoptive fathers had low occupational status; the women generally had had contact with their biological mothers before final placement. Alcohol abuse in the adoptive home did not modify the risk of alcohol abuse in the daughters. As with the study on male adoptees, many women came from families with no history of alcohol abuse.

The most remarkable finding of this study was the strong component of mother-and-

daughter transmission in the adoptee daughters. But the influence may not be purely genetic, since alcohol abuse by the pregnant mother may have affected the growing fetus (the latter would, of course, be true for mother-daughter or mother-son transmission). In the adopted women, both the severity of alcohol abuse and the characteristics of their biological parents resembled those of the Type I male alcohol abusers. The influence of postnatal environment on frequency and severity of abuse could not be conclusively established, however, because of the limitations of the sample population or the failure to identify the relevant variables. Both of these unresolved issues will require further investigation. Nevertheless, the study demonstrated for the first time the existence of a genetic or congenital determinant for alcohol abuse in women.

The demonstration that sociocultural influences are critically important in the majority of genetically predisposed individuals suggests that changes in behavior and social attitudes by and toward individuals at high risk can alter both the course and the prevalence of alcohol abuse and alcoholism. Potential alcohol abusers could be identified through sensitive and accurate physiological, biochemical, and behavioral predictors of alcoholic vulnerability. These recent discoveries are significant for future treatment and prevention strategies as well as for future research on this important health problem. To this end, prospective and longitudinal studies with children of alcoholics, several of which are in progress, offer a promising approach (Schuckit 1980; Gabrielli et al. 1982; Elmasian et al. 1982).

Genetic Factors in Physiological Responses to Alcohol

A number of biological responses to alcohol potentially have pathophysiological significance for alcohol abuse, including

- alcohol craving or alcohol-seeking behavior
- sensitivity of the central nervous system (CNS) to alcohol
- sensitivity of other body systems (systemic sensitivity) to alcohol
- rate of alcohol metabolism or elimination
- rate of acquisition of tolerance to alcohol
- rate of development and severity of physical dependence on alcohol
- susceptibility to the medical complications of chronic alcohol consumption.

Studies in humans and in experimental animals have shown a tremendous degree of individual variation in their biological responses to alcohol. A considerable body of evidence now shows that much of this variation is genetic in origin (McClearn and Erwin 1982). The findings in humans and in experimental animals will be described separately as they use different experimental approaches and design.

Human Studies

Because genes cannot be manipulated in humans, studies have been limited to the comparison of fraternal and identical twins and of different ethnic groups. Identical twins have identical sets of genes, whereas fraternal twins do not. By comparing variability or, conversely, similarity in the expression of a trait within sets of identical and fraternal twins, researchers can determine the heritability or the importance of genes in the expression of that trait. Twin studies are not perfect, however, since the environment of identical twins tends to be more similar than that of fraternal twins. Hence, the extent to which genetic factors affect that trait cannot be established with absolute certainty. A similar limitation pertains to the comparison of different ethnic populations: They differ socioculturally. Accordingly, all candidate genetic traits predisposing to alcohol abuse should be studied in experimental animals so that environmental influences can be experimentally controlled.

Several twin studies have been performed on drinking behavior (Kaij 1960; Partanen et al. 1966; Jonsson and Nilsson 1968; Loehlin 1972; Kaprio et al. 1978). General agreement prevails that genetic factors influence the quantity and frequency of drinking as well as such symptoms of heavy drinking as hangovers and loss of control. Identical twins are more alike than fraternal twins in their drinking behavior, but the environment may play a considerable role.

Twin studies have also been used to demonstrate that neurophysiological sensitivity to alcohol and alcohol elimination rate are genetically controlled. Propping (1977) showed

that alcohol's effects on brain-wave function are nearly identical in identical twins, whereas they are disparate in fraternal twins. Alcohol elimination rate varies by a factor of 2 to 3 among individuals, even after adjustment for body weight (Bennion and Li 1976). Several studies have compared identical and fraternal twins to determine how much genetic factors contribute to this variation (Vesell et al. 1971; Kopun and Propping 1977). Genetic factors account for about 40-50 percent of the variation in alcohol elimination rate. Daily alcohol intake, smoking, diet, and drug use are some of the environmental factors that account for the remainder.

A potential biochemical explanation for genetic variation in human alcohol elimination rate has recently been discovered. Alcohol is eliminated from the body primarily through metabolism. The enzymes or protein catalysts responsible for this process are alcohol dehydrogenase and aldehyde dehydrogenase. The first enzyme oxidizes alcohol to acetaldehyde and the second enzyme oxidizes acetaldehyde to acetate. Acetate then enters the general metabolic pathway for sugars and fats and is oxidized further to carbon dioxide and water (Li 1977). The amount and properties of alcohol dehydrogenase in the liver determine the rate of alcohol metabolism--and there are many genetically disparate forms of this enzyme in human livers, varying among individuals. The individual molecular forms of human liver alcohol dehydrogenase have now been isolated, and many of them differ markedly in their catalytic properties (Bosron and Li 1981). Since the combination of forms is determined genetically, the variation in elimination rate among individuals can be readily accounted for by the large differences in the genetically determined properties of the different enzyme forms. No experiments have yet tried to correlate the specific enzyme makeup of individuals with their alcohol metabolism rates. However, it has been reported that Chinese and Japanese individuals, on the average, metabolize alcohol 30 percent faster than Caucasians do (Hanna 1978). More than 90 percent of Orientals possess the so-called atypical alcohol dehydrogenase genetic trait (Bosron and Li 1981). The atypical alcohol dehydrogenase enzyme forms are much more active than the forms present in Caucasians.

Some individuals, particularly Orientals, respond to alcohol with an "alcohol flush," a systemic reaction consisting of facial flushing and rapid heart rate and, in severe cases, nausea, vomiting, and low blood pressure. For example, approximately half of the Japanese population exhibit the reaction, which has been linked to elevated blood acetaldehyde levels after alcohol intake (Mizoi et al. 1979). Alcohol flush was once thought to be the consequence of an overproduction of acetaldehyde (Stamatoyannopoulos et al. 1975). More recent research, however, indicates that the reaction may result from the absence of a particular form of aldehyde dehydrogenase, thereby affecting the oxidation of acetaldehyde (Inoue et al. 1980; Agarwal et al. 1981; Teng 1981). Indirect evidence suggests that acetaldehyde can cause the release of histamine and perhaps other substances affecting blood vessels; hence, the flush reaction.

Finally, studies of twins have shown that some individuals may be genetically susceptible to certain medical complications of prolonged alcohol abuse, namely liver cirrhosis and psychosis (Hrubec and Omenn 1981). Also, some people may be susceptible to developing the Wernicke-Korsakoff syndrome due to an inherited metabolic defect involving one of the thiamine (vitamin B_1)-requiring enzymes (Blass and Gibson 1977). Studies to confirm these important observations are clearly needed.

Animal Studies

Animals, like humans, vary in their responses to alcohol. Genetic factors are responsible for some of the differences, including such responses to alcohol as the acquisition of tolerance and physical dependence. An important feature of animal experimentation, impossible with humans, is the ability to manipulate the genetic background of the animals through inbreeding, selective breeding, and other measures. It has been possible to develop lines or strains of animals with high or low responsiveness to the various actions of alcohol. Such animals can then be used to study the biochemical and physiological mechanisms underlying genetic variability and to discern how these developed traits and mechanisms affect alcohol-drinking behavior. Conversely, breeders can develop animals that prefer or disdain alcohol, and researchers can test their responsiveness to the various actions of alcohol. Such animal studies can suggest hypotheses and experimental approaches in human research to learn what predisposes individuals genetically to aberrant drinking behavior. Research with animal models thus provides a cornerstone of future biological knowledge

about the nature of genetic susceptibility to alcoholism.

Inbred strains of mice differ in their preference for alcohol consumption when food, water, and alcohol are made freely available to them (McClearn and Rodgers 1959). Inbred mouse strains also differ in "sleep time," that is, the time required to recover from the hypnotic effects of alcohol (Kakihana et al. 1966), and in alcohol metabolic rate (Sheppard et al. 1970). Inbred strains are developed by mating successive generations of close relatives. After about 20 generations of sibling matings, the animals within each inbred strain are almost genetically uniform and show the trait readily. The strains constitute prima facie evidence of genetic influence on that trait.

A genetic influence on alcohol-drinking behavior, CNS sensitivity to alcohol, and alcohol metabolic rate has also been demonstrated in selectively bred lines of rats and mice. Selective breeding is the process by which animals showing a chosen characteristic are mated in successive generations in order to segregate the genes responsible for that trait into one line of animals. Thus, if a quantitative trait is under genetic control, separate strains can be bred, one in the high and the other in the low direction. Rats that differ in alcohol metabolic rate have also been raised through selective breeding (Thurman 1980). Lines of rats have now been bred selectively to differ in voluntary alcohol consumption: the alcohol-preferring AA and P lines and the alcohol-nonpreferring ANA and NP lines (Eriksson 1968; Li et al. 1979). Lines of mice and rats that differ in CNS sensitivity to the sedative-hypnotic effects of alcohol have also been developed: the long-sleep (LS) and short-sleep (SS) mouse lines (McClearn and Kakihana 1973) and the most-affected (MA) and least-affected (LA) lines of rats (Riley et al. 1977). Such selectively bred animals are particularly useful for studying the underlying mechanisms that contribute to these genetic differences. For example, the difference in sleep time between the LS and SS mice is related to a genetically determined difference in the brain that is both region-specific and drug-specific (Sorensen et al. 1981). New and exciting findings are likely to emerge from further studies with these animals that will improve reseachers' understanding of the differential CNS sensitivity to alcohol in humans.

Various inbred strains of mice as well as the selectively bred LS and SS lines of mice differ in how rapidly they develop tolerance after the chronic administration of alcohol (Grieve et al. 1979; Tabakoff et al. 1980). Inbred mouse strains also differ in the severity of withdrawal symptoms after physical dependence has been established. Goldstein (1973) and Goldstein and Kakihana (1974) bred mouse lines with those reactions. Thus, both the rate of tolerance development and the severity of physical dependence caused by chronic alcohol ingestion are genetically determined in mice and possibly in humans.

Potential Mechanisms of Genetic Influence

Alcoholism and alcohol abuse lie at one extreme of a continuum of drinking behavior whose opposite end represents abstinence. Drinking behavior as a trait, therefore, is a continuous variable, as are height and weight. Such traits are usually determined by many sets of genes that sometimes tend to appear together or to be correlated. When different traits can be influenced by common sets of genes, a phenomenon called pleiotropy, true genetic correlation has occurred. The association may come about because one trait influences the expression of the other. For example, preliminary reports from Japan indicate that, compared with the normal population, alcoholic populations contain fewer individuals with deficiencies in the mitochondrial enzyme aldehyde dehydrogenase that oxidizes acetaldehyde (Harada et al. 1982; Yoshihara et al. 1982). When this enzyme is absent, alcohol consumption leads to high blood acetaldehyde levels and the unpleasant alcohol flush reaction. Thus, an individual with the enzyme deficiency is likely to avoid alcohol and the unpleasant reaction it brings.

Animal studies have revealed other potential mechanisms of genetic influence. Mice that consume large amounts of alcohol voluntarily are more likely than others to acquire tolerance rapidly (Erwin et al. 1980). Alcohol-preferring lines of rats recover more rapidly from the sedative-hypnotic effects of alcohol than do alcohol-nonpreferring ones (Lumeng et al. 1982). These studies suggest an experimentally verifiable hypothesis: An ability to adapt quickly to alcohol (tolerance) may predispose individuals to patterns of heavy drinking.

Other mechanisms of alcohol preference are likely to be discovered, each of which may contribute in some way to the trait of high voluntary alcohol consumption. Animal exper-

iments can reveal such mechanisms of alcohol consumption (NIAAA 1981). This research approach may ultimately lead to an understanding of the nature of genetic heterogeneity of alcohol abuse and alcoholism in humans, the physiological and biochemical mechanisms underlying this problem behavior, and how environmental factors interact with these inherited pathways.

Summary

Great strides have been made in recent years in researchers' knowledge and understanding of the genetic factors contributing to alcohol abuse and alcoholism. It has been firmly established that heredity plays a role in determining individual differences in susceptibility to the disorder. Genetic influence is identifiable in at least 35 to 40 percent of alcoholics and alcohol abusers, and it affects both men and women. People with family histories involving parental alcohol abuse face increased risk. Furthermore, many types of alcohol abuse may exist, each with its own genetic predisposition interacting with a particular environment.

Genetic factors also affect individual differences in response to alcohol, such as drinking behavior, sensitivity of the brain and other body systems to alcohol, alcohol elimination rate, the acquisition of tolerance, and the development of physical dependencies. Much of this knowledge has been obtained from experiments in laboratory animals specifically developed for the purpose of alcoholism-related research.

Collectively, the gains in research in the past decade predict an exciting era of new discoveries in the next. Future research should focus on improving methodology for detecting subtypes of alcohol abuse and on developing behavioral, physiological, and biochemical predictors of genetic vulnerability. In this regard, ongoing and future work in experimental animals can provide invaluable clues for human investigation. Existing animal models and those yet to be developed can be used not only to identify genetic correlates of alcohol-seeking behavior, but also to elucidate the biological nature of the process. When this stage of knowledge is reached, the genetic subtypes of alcohol abuse and alcoholism will be precisely defined as pharmacogenetic disorders of behavior by the nature of their underlying pathology.

References

Agarwal, D.P.; Harada, S.; and Goedde, H.W. Racial differences in biological sensitivity to ethanol: The role of alcohol dehydrogenase and aldehyde dehydrogenase isoenzymes. Alcoholism: Clinical and Experimental Research 5:12-16, 1981.

Bennion, L.J., and Li, T.-K. Alcohol metabolism in American Indians and whites. New England Journal of Medicine 294:9-13, 1976.

Blass, J.P., and Gibson, G.E. Abnormality of a thiamine-requiring enzyme in patients with Wernicke-Korsakoff syndrome. New England Journal of Medicine 297:1367-1370, 1977.

Bohman, M. Some genetic aspects of alcoholism and criminality: A population of adoptees. Archives of General Psychiatry 35:269-276, 1978.

Bohman, M.; Sigvardsson, S.; and Cloninger, C.R. Maternal inheritance of alcohol abuse: Cross-fostering analysis of adopted women. Archives of General Psychiatry 38:965-969, 1981.

Bosron, W.F., and Li, T.-K. Genetic determinants of alcohol and aldehyde dehydrogenases and alcohol metabolism. Seminars in Liver Disease 1:179-188, 1981.

Cadoret, R.J., and Gath, A. Inheritance of alcoholism in adoptees. British Journal of Psychiatry 132:252-258, 1978.

Cadoret, R.J.; Cain, C.A.; and Grove, W.M. Development of alcoholism in adoptees raised apart from alcoholic biologic relatives. Archives of General Psychiatry 37: 561-563, 1980.

Cloninger, C.R.; Bohman, M.; and Sigvardsson, S. Inheritance of alcohol abuse: Cross-fostering analysis of adopted men. Archives of General Psychiatry 38:861-868, 1981.

Cotton, N.S. The familial incidence of alcoholism. Journal of Studies on Alcohol 40: 89-116, 1979.

Elmasian, R.; Neville, H.; Woods, D.; Schuckit, M.; and Bloom, F. Event-related brain potentials are different in individuals at high risk and low risk for developing alcoholism. Proceedings of the National Academy of Sciences 79:7900-7903, 1982.

Eriksson, K. Genetic selection for voluntary alcohol consumption in the albino rat. Science 159: 739-741, 1968.

Erwin, V.G.; McClearn, G.E.; and Kuse, A.R. Interrelationships of alcohol consumption, actions of alcohol and biochemical traits. Pharmacology, Biochemistry and Behavior 13(Supplement 1): 297-302, 1980.

Feighner, J.; Robins, E.; Guze, S.; Woodruff, R.; Winokur, G.; and Munoz, R. Diagnostic criteria for use in psychiatric research. Archives of Gen-

eral Psychiatry 26:57-63, 1972.

Gabrielli, W.F.; Mednick, S.A.; Volavka, J.; Pollock, V.E.; Schulsinger, F.; and Itil, T.M. Electroencephalograms in children of alcoholic fathers. Psychophysiology 19:404-407, 1982.

Goldstein, D.B. Inherited differences in intensity of alcohol withdrawal reactions in mice. Nature 245:154-156, 1973.

Goldstein, D.B., and Kakihana, R. Alcohol withdrawal reactions and reserpine effects in inbred strains of mice. Life Science 15: 415-425, 1974.

Goodwin, D.W. Is alcoholism hereditary? A review and critique. Archives of General Psychiatry 25:545-549, 1971.

Goodwin, D.W.; Schulsinger, F.; Hermansen, L.; Guze, S.B.; and Winokur, G. Alcohol problems in adoptees raised apart from alcoholic biological parents. Archives of General Psychiatry 28:238-243, 1973.

Goodwin, D.W.; Schulsinger, F.; Hermansen, L.; Guze, S.B.; and Winokur, G. Alcoholism and the hyperactive child syndrome. Journal of Nervous and Mental Disease 160:349-353, 1975.

Goodwin, D.W.; Schulsinger, F.; Knop, J.; Mednick, S.; and Guze, S.B. Alcoholism and depression in adopted-out daughters of alcoholics. Archives of General Psychiatry 34:751-755, 1977.

Goodwin, D.W.; Schulsinger, F.; Moller, N.; Hermansen, L.; Winokur, G.; and Guze, S.B. Drinking problems in adopted and nonadopted sons of alcoholics. Archives of General Psychiatry 31:164-169, 1974.

Grieve, S.J.; Griffiths, P.J.; and Littleton, J.M. Genetic influences on the rate of development of ethanol tolerance and the ethanol physical withdrawal syndrome in mice. Drug and Alcohol Dependence 4:77-86, 1979.

Hanna, J.M. Metabolic response of Chinese, Japanese and Europeans to alcohol. Alcoholism: Clinical and Experimental Research 2:89-92, 1978.

Harada, S.; Takagi, S.; Agarwal, D.P.; and Goedde, H.W. Ethanol and aldehyde metabolism in alcoholics from Japan (abstract). Alcoholism: Clinical and Experimental Research 6:298, 1982.

Hrubec, Z., and Omenn, G.S. Evidence of genetic predisposition to alcoholic cirrhosis and psychosis: Twin concordances for alcoholism and its biological end points by zygosity among male veterans. Alcoholism: Clinical and Experimental Research 5:207-215, 1981.

Inoue, K.; Fukunaga, M.; and Yamasawa, K. Correlation between human erythrocyte aldehyde dehydrogenase activity and sensitivity to alcohol. Pharmacology, Biochemistry and Behavior 13:295-297, 1980.

Jonsson, E., and Nilsson, T. Alcohol konsumption hos monozygota och dizygota tvillingpar. Nordisk Hygienisk Tidskrift 49:21-25, 1968.

Kaij, L. Alcoholism in Twins. Studies on the Etiology and Sequels of Abuse of Alcohol. Stockholm: Almqvist and Wiksell, 1960.

Kakihana, R.; Brown, D.R.; McClearn, G.E.; and Tabershaw, I.R. Brain sensitivity to alcohol in inbred mouse strains. Science 154:1574-1575, 1966.

Kaprio, J.; Sarna, S.; Koskenvuo, M.; and Rantasalo, I. The Finnish Twin Registry: Baseline Characteristics. *Section II. History of symptoms* and illnesses, use of drugs, physical characteristics, smoking, alcohol and physical activity. Kansanterveystieteen Julkaisuja M 37, Helsinki, 1978.

Kopun, M., and Propping, P. The kinetics of ethanol absorption and elimination in twins and supplementary repetitive experiments in singleton subjects. European Journal of Clinical Pharmacology 11:337-344, 1977.

Li, T.-K. Enzymology of human alcohol metabolism. Advances in Enzymology 46:427-483, 1977.

Li, T.-K.; Lumeng, L.; McBride, W.J.; and Waller, M.B. Progress toward a voluntary oral consumption model of alcoholism. Drug and Alcohol Dependence 4:45-60, 1979.

Loehlin, J.C. An analysis of alcohol-related questionnaire items from the National Merit Twin Study. In: Seixas, F.A.; Omenn, G.S.; Burk, E.D.; and Eggleston, S., eds. Vol. 197, Nature and nurture in alcoholism. Annals of the New York Academy of Science 197:117-120, 1972.

Lumeng, L.; Waller, M.B.; McBride, W.J.; and Li, T.-K. Different sensitivities to ethanol in alcohol-preferring and nonpreferring rats. Pharmacology, Biochemistry and Behavior 16:125-130, 1982.

McClearn, G.E., and Erwin, V. Mechanisms of genetic influence on alcohol-related behaviors. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM)82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 263-289.

McClearn, G.E., and Kakihana, R. Selective breeding for ethanol sensitivity in mice. Behavioral Genetics (abstract) 3:409-410, 1973.

McClearn, G.E., and Rodgers, D.A. Differences in alcohol preference among inbred strains of mice. Quarterly Journal of Studies on Alcohol 20:691-695, 1959.

Mizoi, Y.; Ijiri, J.; Tatsuno, Y.; Kijima, T.; Fujiwara, S.; and Adachi, J. Relationship between facial flushing and blood acetaldehyde levels after ethanol intake. Pharmacology, Biochemistry and Behavior 10:303-311, 1979.

National Institute on Alcohol Abuse and Alcoholism. Development of Animal Models as Pharmacogenetic Tools. NIAAA Research Monograph No. 6. McClearn, G.E.; Deitrich, R.A.; and Erwin, V.G., eds. DHHS Pub. No. (ADM)81-1133. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

Partanen, J.K.; Bruun, K.; and Markkanen, T. Inheritance of Drinking Behavior. A Study on Intelligence, Personality and Use of Alcohol in Adult Twins. Finnish Foundation for Alcohol Studies Pub. No. 14. Helsinki: Finnish Foundation for Alcohol Studies, 1966.

Propping, P. Genetic control of ethanol action on the central nervous system. Human Genetics 35:309-334, 1977.

Riley, E.P.; Worsham, E.D.; Lester, D.; and Freed, E.X. Selective breeding of rats for differences in reactivity to alcohol: An approach to an animal model of alcoholism. II. Behavioral measures. Journal of Studies on Alcohol 38: 1705-1717, 1977.

Roe, A. The adult adjustment of children of alcoholic parents raised in foster homes. Quarterly Journal of Studies on Alcohol 5:378-393, 1944.

Schuckit, M.A. Biological markers: Metabolism and acute reactions to alcohol in sons of alcoholics. Pharmacology, Biochemistry and Behavior 13(Supp. 1): 9-16, 1980.

Schuckit, M.A.; Goodwin, D.A.; and Winokur, G. A study of alcoholism in half siblings. American Journal of Psychiatry 128:1132-1136, 1972.

Sheppard, J.R.; Albersheim, P.; and McClearn, G.E. Aldehyde dehydrogenase and ethanol preference in mice. Journal of Biological Chemistry 245:2876-2882, 1970.

Sorensen, S.; Dunwiddie, T.; McClearn, G.; Freedman, R.; and Hoffer, B. Ethanol-induced depressions in cerebellar and hippocampal neurons of mice selectively bred for differences in ethanol sensitivity: An electrophysiological study. Pharmacology, Biochemistry and Behavior 14: 227-234, 1981.

Stamatoyannopoulos, G.; Chen, S.-H.; and Fukui, M. Liver alcohol dehydrogenase in Japanese: High population frequency of atypical form and its possible role in alcohol sensitivity. American Journal of Human Genetics 27:789-796, 1975.

Tabakoff, B.; Ritzmann, R.; Raju, T.S.; and Deitrich, R.A. Characterization of acute and chronic tolerance in mice selected for inherent differences in sensitivity to ethanol. Alcoholism: Clinical and Experimental Research 4:70-73, 1980.

Teng, Y.-S. Human liver aldehyde dehydrogenase in Chinese and Asiatic Indians: Gene deletion and its possible implications in alcohol metabolism. Biochemical Genetics 19:107-114, 1981.

Thurman, R.G. Ethanol elimination rate is inherited in the rat. In: Thurman, R.G., ed. Alcohol and Aldehyde Metabolizing Systems - IV. Advances in Experimental Medicine and Biology Vol. 132. New York: Plenum Press, 1980. pp. 655-661.

Vesell, E.S.; Page, J.G.; and Passananti, G.T. Genetic and environmental factors affecting ethanol metabolism in man. Clinical Pharmacology and Therapeutics 12:192-201, 1971.

Yoshihara, H.; Sato, N.; Kamada, T.; and Abe, H. Low K_m ALDH isozyme and alcoholic liver injury (abstract). Alcoholism: Clinical and Experimental Research 6:319, 1982.

Chapter III

Psychobiological Effects of Alcohol

Alcohol acts on virtually every cell of the body, but the central nervous system is the target most affected. Alcohol's influence is profound--from the personality disarray created by chronic drinking to the distorted judgment of the drunken driver. Current research is converging on explanations for some of these effects and their underlying biological mechanisms, but a comprehensive understanding of an individual's response to alcohol is still elusive.

Because no unitary explanation of alcohol's effect on human behavior seems adequate, researchers continue to explore all levels of brain function and behavior. Accordingly, this chapter presents selected research findings at four broad levels--cognition and neuropsychological effects, neuropathological illness, electrophysiology, and neural and biochemical effects. Finally, a brief overview of theories that may explain the appeal of alcohol and the causes of alcohol addiction are discussed.

Cognitive and Neurophysiological Effects

Driving-Related Cognitive Skills

Our society has acknowledged the profound and often harmful behavioral effects of alcohol, especially as it involves drinking and driving. Driving is a complex task requiring such skills as psychomotor coordination, reaction time, memory, perception, judgment, information processing, and conscious control of behavior. Not surprisingly, many researchers have chosen to investigate alcohol's cognitive effects by measuring how it impairs various driving-related skills. Such studies can yield practical applications while also revealing more basic psychological mechanisms.

Clayton (1980) found that driving skills are impaired at blood alcohol concentrations (.04-.05 percent) one might observe after drinking only two to three alcoholic beverages on an empty stomach. In addition, he found that the same blood alcohol level decreased a driver's ability to divide his attention among several stimuli while maintaining acceptable performance. Clayton suggested that the resulting diminished performance could be caused by a decreased ability to process information.

Driving a car is a learned skill that requires good judgment based on experience and practice. McNamee et al. (1980) examined how alcohol affects experience and judgment in estimating the velocity of a moving object--an essential task for drivers. Initially, with low doses of alcohol, the subjects actually improved their estimates. But after continuing to drink (resulting in a blood alcohol concentration above .10 percent), their performance declined dramatically. This biphasic phenomenon, of initial stimulation or excitation of the central nervous system with low doses followed by depression as the dose is increased, will be encountered again later in this chapter.

In a study closely related to velocity estimates, Colins and Chiles (1980) investigated how alcohol affects tracking skills in airline pilots. The results confirmed McNamee's study and showed, in addition, that the pilot's errors were greatest and most frequent during evening hours. Thus, it appears that biological rhythms may influence alcohol's effects on judgment. The researchers also found that many hours of abstinence are required to eliminate all such alcohol-induced errors.

Many people believe they can override or control alcohol's negative effects on behavior. Young and Pihl (1980) evaluated the degree to which volunteer subjects could control their speech and behavior and prevent visible symptoms of intoxication. Although the subjects varied greatly in their suppression of symptoms, none was completely successful.

Fatigue impairs cognitive performance in much the same way that alcohol does, leading some researchers to examine the relationship between the two. Ryder et al. (NHTSA 1981)

reported that alcohol increased the cognitive impairments produced by fatigue as determined by driving performance. Caffeine is thought by many to counteract the effects of both alcohol and fatigue. Moskowitz and Burns (1981), using a driving simulator, evaluated caffeine as a possible antidote to alcohol in tracking, searching, and information processing. They found that caffeine could partially counteract the behavioral effects of alcohol. However, since the effects were marginal, these findings should discourage the folk belief that coffee is an effective antidote to alcohol, especially when driving. In a study of another often-used combination, Tong et al. (1980) found that both tobacco and alcohol individually diminished auditory vigilance (ability to detect sound stimuli); taken together, they led to even greater impairments.

Using an animal research design that is likely to reflect human reactions, Moody et al. (1980) demonstrated that alcohol significantly slowed monkeys' reaction time to sound signals. Recordings of electrical activity in the brain's auditory pathways showed that alcohol had not impeded the signal from the ear to the brain. Rather, the impairment seemed to be caused by slow information processing in the brain's "higher" centers.

Cognitive Functioning in Social Drinkers

Since this topic was reviewed in previous reports to Congress (USDHHS 1981; Parsons and Leber 1982), MacVane et al. (1982) have also found that performance on some neuropsychological tests correlates with social drinking patterns. Five studies have found some statistical relationships between alcohol use and decreased cognitive performance in social drinkers (Parker 1982). However, as Parsons and Fabian (1982) have pointed out, such relationships were not consistent for the same cognitive tests in each of these studies. Furthermore, in the MacVane study, although the 58 heavy social drinkers drank three times as often and twice as much as did the 48 light-moderate drinkers, the performance of the two groups on the cognitive tests was not significantly different.

Methodologic issues may partially explain the lack of a dose-response relationship between consumption and cognitive ability (Parker 1982). However, variables other than alcohol use, as yet unknown, may also be involved (Parsons and Fabian 1982). Individuals with poor cognitive function, for example, may drink more than those with high functioning; the former, due to poor verbal skills, may provide less valid drinking histories. Heavy drinkers may be more anxious and depressed perhaps due to underlying problems or the recency of drinking. Finally, individuals may have to consume a minimal amount of alcohol (threshold) before it has detrimental effects.

As more sensitive techniques for assessing neuropsychological functioning have been applied to individuals with differing social drinking patterns and socioeconomic circumstances, it has become increasingly clear that many questions must be answered. Specifically, what are the limits of normal functioning? At what point should an individual be considered impaired due to alcohol use? Is alcohol use a causative or an exacerbating factor, a complication of or simply coincidental to such measured impairments? The social use of alcohol is sufficiently widespread in our culture, and the degree of behavioral impairment attributed to social drinking is difficult to measure. Therefore, long-term studies of many individuals with varied drinking patterns will be needed to clarify the cognitive consequences of social drinking.

Alcohol and Aging

On average, older persons perform less well on standard psychological tests than younger ones with equivalent patterns of alcohol consumption (Carlen et al. 1981b). However, people of the same chronologic age may age quite differently physiologically.

Because young alcoholics resemble old people in their performance on neuropsychological tests, some researchers have hypothesized that alcohol consumption may accelerate the normal process of aging (Ryan 1982). However, electrophysiologic data, particularly brain evoked potentials (electrical activity in response to sensory stimulation), suggest that the organic brain disease of alcoholics is caused by an underlying mechanism different from premature aging (Porjesz and Begleiter 1982).

Whether or not the two processes share a common cause, alcohol consumption may interact with aging in several ways (Freund and Butters 1982). Changes in their ability to metabolize alcohol and in their central nervous system function may make the elderly increasingly vulnerable to the deleterious effect of alcohol (Wood and Armbrecht 1982). In addition, alcohol may interfere with normal

regenerative processes of the central nervous system (West et al. 1982).

Alcoholics Versus Nonalcoholics

All of the previously discussed human studies examined alcohol's effects on the behavior of individuals from the population at large. But the population includes both alcoholics and nonalcoholics, who may respond to alcohol differently. Recent research has attempted to measure alcohol's cognitive and neuropsychologic effects on alcoholics compared with nonalcoholics. Further, it has examined both the effects of acute (short-term) doses of alcohol and the impact of chronic drinking.

Cognitive Effects of Alcoholism

O'Leary et al. (1980) found that alcoholics performed significantly worse than did nonalcoholics when tested for their ability to note and distinguish slight differences between closely related objects. In a study that could explain the results obtained by O'Leary and his associates, Rubin (1980) found that, compared with nonalcoholics, alcoholics exhibit various autonomic nervous system difficulties, including poor physiological regulation of eye pupil size and the rate at which pupils respond to visual stimuli. Such poor regulation could hamper alcoholics in distinguishing between closely related objects.

Several studies have suggested that while alcoholism does impair cognitive skills, alcoholics regain such skills quite rapidly after they stop drinking. Chaney et al. (1980) confirmed the earlier studies, adding that younger alcoholics regain their verbal skills after detoxification more rapidly than do older alcoholics.

Ryan (1980) found that, at the beginning of a testing session, alcoholics and nonalcoholics performed equally well in a short-term memory test. But, when asked to recall words after a 3-hour interval, the alcoholics remembered significantly fewer words than did the nonalcoholics, possibly as a result of more mental fatigue.

Neuropsychological Performance in Alcoholics

Brain abnormalities underlie cognitive impairment in alcoholics (Wilkinson 1982). In the largest long-term study of computer-assisted tomography (brain scan) changes in alcoholics, all brain scan measurements differed significantly between alcoholics and controls. None of the alcoholics had clinically overt signs of brain damage, but all showed the syndrome of alcohol dependence (Ron et al. 1982).

Alcoholics over 43 years of age differed from their controls more markedly than did the younger alcoholics. Brain scan measurements were significantly correlated with age, but not with such measures of alcoholism as length of drinking history, measures of amount consumed, or scores on a "social decline scale."

In the older subjects, abnormalities seen by brain scans were least severe in those who had abstained longest before scanning. In addition, it was noted that recovery proceeded at a faster rate in younger alcoholics compared with older alcoholics. In followup tests, from 30 weeks to 3 years after initial examination, the largely abstinent patients showed significant improvement over time in brain scans, while the continuing drinkers showed little change. The length of abstinence was correlated with the degree of improvement.

The work of Ron and his colleagues (1982) suggests that neuropsychologic deficits may be reversible. However, Adams et al. (1980) were unable to demonstrate improved neuropsychological performance in patients in their late thirties from an alcoholism treatment program tested 3 weeks after their last drink and again 1 year later. Posttreatment alcohol consumption by 63 percent of these patients may have influenced this study, however, as Eckardt et al. (1980) noted that abstainers perform better than those who resume alcohol consumption. These results emphasize that total abstinence is desirable if alcohol-related cognitive deficits are to be reversed. Reviews of existing literature noted, however, that many studies fail to assess alcohol intake accurately during so-called periods of abstinence (Orrego et al. 1979; Parsons and Leber 1982).

Nutrition and Alcoholism

Because alcohol is a concentrated source of energy (about 200 calories per ounce), alcoholics often find their caloric needs largely satisfied by the alcohol they consume but develop deficiencies of vital nutritional elements. Indeed, most medical textbooks recommend restoration of a proper diet with vitamin supplementation as a first-order treatment of alcoholism. In particular, thia-

mine (vitamin B_1) deficiency may result in the damage to brain cells (Blass 1980), and alcohol itself may interfere with thiamine's absorption from the gastrointestinal tract (Hoyumpa 1980).

A genetic enzyme abnormality may largely determine which individuals are most likely to become thiamine deficient during periods of poor nutrition (Leigh et al. 1981). Shaw and his associates (1981) reported impaired learning in thiamine-deficient rats, but not in rats fed a balanced diet or an alcohol-containing liquid diet. Thus, it appeared that thiamine deficiency alone can cause neuropsychological damage.

Other evidence (Walker et al. 1981), however, suggests that, despite adequate diet, chronic alcohol consumption is in itself neurotoxic and causes learning deficits as well as long-lasting brain damage. Clearly, both nutrition and alcohol contribute to neurotoxicity, and their relative roles in alcoholic brain injury remain to be resolved.

Neuropathologic Illnesses

Chronic Organic Brain Syndromes

Chronic consumption of harmful quantities of alcohol may lead to two clinically and neuropathologically distinguishable chronic organic brain syndromes: alcoholic dementia and alcohol amnestic (memory loss) syndrome (also called Korsakoff's psychosis) (Wilkinson and Carlen 1981; Lishman 1981).

Chronic organic brain syndromes due to alcoholism are the second most common of the known causes of dementia in adults (approximately 10 percent) next to Alzheimer's disease (40-60 percent) (Wells 1979). Despite emerging technological advances, a large proportion of dementing illnesses can be diagnosed with certainty only by examining the microscopic structure of the brain at autopsy. For example, alcoholic dementia is characterized pathologically by destruction of cerebral cortical neurons, particularly those in the frontal lobes.

The clinical picture of alcoholic dementia may be indistinguishable from that of Alzheimer's disease. Global intellectual decline, seen in both, is characterized by deficits in abstracting ability and problem solving, dysphasia (deficit in verbal expression), and apraxia (diminished skill in motor tasks). Electroencephalographic (EEG) abnormalities, cerebral and cerebellar tissue loss, and the enlargement of the fluid spaces in the interior of the brain are also similar in the two disorders. But the overall course of the diseases is potentially different. In alcoholic dementia, cognitive impairment is reversible to some degree with abstinence, although cognitive decline usually occurs with continued drinking (Cutting 1978). Potential reversibility clearly differentiates alcoholic dementia from Alzheimer's disease, which is invariably progressive. Gottfries (1980) suggests that alcoholic dementia may be differentiable from Alzheimer's disease on the basis of abnormal acetylcholine neurotransmission in the latter. This may be difficult to demonstrate, however, due to the many areas of neurochemical overlap among Alzheimer's disease, alcoholic dementia, and aging.

Patients with Korsakoff's psychosis (see USDHHS 1981; Butters 1982), unlike those with alcoholic dementia, suffer severe and often persistent memory impairment while other intellectual functions remain relatively intact. There are marked deficits in acquiring new learning and amnesia for more recent events. Unlike early-stage Alzheimer patients with superficially similar memory deficits, Korsakoff patients can recall rules for organizing information and can recall previously acquired knowledge (Weingartner et al. 1983). At autopsy, Korsakoff patients have characteristic lesions that resemble those described in patients who have died from acute thiamine deficiency (Wernicke's encephalopathy). Those lesions, whose precise relationship to the Korsakoff memory deficits is still controversial (Butters 1982), are near brain pathways that in animal studies have been implicated in learning, memory, drive, and reward. Mair et al. (1982) have found reductions in neurotransmitters, which are correlated with the performance of Korsakoff patients on learning tasks. However, it is unclear whether such neurochemical changes are significantly different from those seen in age-matched healthy controls or in individuals with dementia due to other causes.

Harper (1979) diagnosed 51 cases with the pathological findings of Wernicke's encephalopathy (thiamine-related degeneration of neurons in the brain) or approximately 2 percent of the brains examined from diseased alcoholics at autopsy in a 4-year study. These findings were not appreciably different from those of similar prior studies (Cravioto et al. 1961; Victor et al. 1971). In only 7 of Harper's

51 cases had the clinical diagnosis of Wernicke's encephalopathy or Korsakoff's psychosis been considered during life. The majority of affected patients were known alcoholics; 10 had died suddenly and unexpectedly, apparently as a result of hemorrhages in the part of the brain that controls the heart rate and respiration.

It is disturbing that Wernicke's encephalopathy is so greatly underdiagnosed because it is treatable and preventable with adequate thiamine supplementation. Harper (1979) and Lishman (1981) suggest that the present clinical appearance of Wernicke encephalopathy and Korsakoff syndrome may have changed somewhat from classical descriptions because many alcoholics may now routinely receive thiamine treatment before the clinical signs are obvious. Such treatment, while insufficient to prevent the disease, masks the classical syndrome, thereby making a traditional diagnosis difficult. Thus, clinical symptoms may develop after repeated episodes of barely detectable brain degeneration in which the usual signs of mental confusion, ataxia (loss of body coordination), ophthalmoplegia (eye paralysis), nystagmus (abnormal eye movements), and memory loss are absent or not readily recognized (Kearsley and Musso 1980).

In alcoholics, Alling and Bostrom (1980) have found damage to myelin, the covering sheaths that enhance electrical conduction in some nerve cells. The damage occurred in a part of the brain almost always affected in classical Korsakoff's psychosis. These randomly selected alcoholics never had Wernicke encephalopathy or Korsakoff syndrome in life and did not show the typical pathologic changes of this disorder under microscopic examination at autopsy.

Alcoholic dementia and Korsakoff's psychosis probably represent ends of a continuum, with the majority of patients seen in clinical practice falling somewhere in between and having some characteristics of both (Parsons and Leber 1982; Butters 1982; Harper 1982). It is not uncommon to find the symptoms of alcoholic dementia (cortical atrophy, enlarged fluid space in the interior of the brain, and moderate intellectual decline) in patients with Korsakoff's psychosis. Conversely, those with alcoholic dementia probably have some memory loss and frequently have microscopic findings that are characteristic of Korsakoff's psychosis. Both nutritional deficits and alcohol neurotoxicity may contribute to either chronic organic brain syndrome.

Relationship Between Alcohol Abuse and Psychiatric Illnesses

Drinking in sufficient amounts to cause serious medical, social, domestic, vocational, or legal problems may reflect, occur together with, or lead to various psychiatric illnesses (Martin 1981). Alcohol use itself may produce various forms of psychopathology as a direct result of its pharmacologic actions (Behar and Winokur 1979), through psychosocial consequences of its chronic use (Goodwin and Guze 1979), or by alteration of psychological equilibrium during alcohol withdrawal (Hamm et al. 1979). Depression, anxiety, hysteria, sociopathy, drug abuse, anorexia nervosa, and childhood hyperactivity are more common in alcoholics and in their family members than in the general population (Morrison and Stewart 1971; Overall et al. 1973; Goodwin et al. 1975; Tarter et al. 1977; Andreasen and Winokur 1979; Eckert et al. 1979; Goodwin and Guze 1979; Munjack and Moss 1981; Wood et al. 1983).

Whether psychopathology is the result of, or the cause of, alcoholism is sometimes difficult to determine. There are, however, definite clinical implications for each alternative (Andreasen and Winokur 1979; Hamm et al. 1979; Weissman and Myers 1980; Linnoila and Martin 1983). For example, if alcoholism predates psychiatric symptoms, abstinence from alcohol is indicated before beginning other treatments (Schuckit 1982). If the alcoholism follows psychiatric disease, it is important to diagnose the psychiatric illness accurately so that treatment may be tailored to the patient's needs (Linnoila and Martin 1983).

The considerable overlap between alcoholism and the affective disorders (mania and depression) has become an important area of research. Alcoholism and depression are the two behavior-associated illnesses with the highest rates of suicide (Tsuang 1977). Recent evidence suggests possible common abnormalities in metabolism of the neurotransmitter serotonin in alcoholism, aggression, suicide, and depression (Ballenger et al. 1979; Rosenthal et al. 1980; Brown et al. 1982). Such neurochemical similarities between alcoholism and depression suggest that there may be a common underlying mechanism. Tricyclic antidepressants and lithium—medications for depression and mania—may offer significant therapeutic benefit to alcoholics who are depressed (Coppen 1980).

Indirect Alcohol-Induced Neuropathology

Liver disease associated with alcoholism may result in behavioral deficits ranging from subtle neuropsychologic abnormalities (Smith and Smith 1977; Rehnstrom et al. 1977) to serious brain degeneration, delirium, and coma (Schenker et al. 1980). In addition, head trauma and inadequate oxygen supply to the brain, frequently sustained during intoxication, can become a recurrent theme in the life of an alcoholic, with cumulative and adverse neurologic effects (McLeod 1982).

Alcohol inhibits the respiratory center of the brain and renders the individual more susceptible to obstructive sleep apnea (inability to breathe normally during sleep), an increasingly recognized condition that causes hypoxemia (reduced blood oxygen content) during sleep (Guilleminault et al. 1978). Even mild hypoxemia may adversely affect brain function and lead to dementia, particularly in individuals who have chronic obstructive lung disease, as is often the case in alcoholics (Blass 1980).

Hillbom and Kaste (1982) have reported that both occasional alcohol intoxication and regular heavy drinking carry an increased risk of stroke due to subarachnoid hemorrhage, but the mechanism for this is not yet clear. In addition, alcohol withdrawal may be accompanied by serious metabolic disturbances that can impair cerebral function (Linnoila and Martin 1983).

The common use of other psychoactive drugs by alcoholics may also contribute to behavioral deficits (Linnoila and Martin 1983). Depression, which frequently accompanies harmful alcohol use (Schuckit 1982), can also impair cognition considerably (Weingartner et al. 1981). Cognitive impairment may often precede alcoholism, however. The high prevalence of attention disorders in young male alcoholics (Wood et al. 1983), for example, suggests that part of the cognitive impairment attributed to alcohol-related brain damage was probably present before the use of alcohol (Parsons and Leber 1982).

Electrophysiology

Increasingly over the past half century, electrophysiological recordings have been expanding researchers' knowledge of the nervous system. Until about 25 years ago, such recordings were limited to macroelectrodes, large probes that recorded only gross brain activities of thousands or even millions of nerve cells. The recordings, called electroencephalograms (EEGs), could indicate the results of either spontaneous brain activity or the brain's responses to a stimulus such as a light flash (evoked potentials). More recent technological advances allow microrecordings from single nerve cells. In today's research, both macro- and microrecordings of alcohol's effects augment one another to contribute to an understanding that neither alone can provide.

In general, the electrophysiological effects of alcohol are complex and vary at different sites within the brain. Most alcohol research with these techniques has attempted to determine functional central nervous system differences between alcoholics and nonalcoholics and, sometimes, to quantify the acute effects of alcohol.

EEG Studies

Recent studies have compared EEGs accompanying the loss of consciousness resulting from alcohol ingestion, normal sleep, and barbiturates (Zornetzer et al. 1982). Although the loss of consciousness caused by most barbiturates and by alcohol superficially resembles normal sleep, the conditions are quite different electrophysiologically.

Surprisingly little detailed information exists on how acute doses of alcohol affect the EEG. Several recent studies have investigated the relation between alcohol's effects on the cortical (outer brain layer) EEG and its effects on EEGs from deep brain structures. Grupp (1981) reported that alcohol altered the electrical activity of both the hippocampus (a deep brain structure associated with memory and emotion) and the cerebral cortex (involved in high-level information processing). Partly on the basis of such studies, Klemm and Sherry (1981) proposed a brain model of intoxication. They theorized that alcohol "scrambles" brain messages, thus disrupting normal communication within the central nervous system. Because Klemm and Sherry rely largely on supporting evidence recorded from the cerebellum (a part of the brain associated with posture, movement, and balance), their model may not account for the pervasive effects of intoxication on other brain structures.

Evoked Response Studies

Electrophysiological responses to sensory stimuli reveal a great deal about the brain.

Because responses to individual stimuli are often lost in a sea of electrical "noise," however, researchers often resort to a technique called the average evoked response (AER). In essence, a readable AER depends on a computer's averaging a large number of the brain's electrical responses to repetitive sensory stimuli. Individual responses that would be imperceptible without computer assistance become magnified and visible when averaged together.

Recently, several researchers have turned to the AER to investigate the brain's response to sensory stimuli under various conditions of alcohol use. Studies showed that alcohol disrupted (1) the normal AERs to visual stimuli (Hetzler et al. 1980); (2) the normal patterns of attention to visual stimuli (NHTSA 1980); and (3) the normal AERs to auditory stimuli (Pfefferbaum et al. 1980), which were correlated with slowed reaction times to sound signals. Such disrupted electrophysiological responses to perceptual stimuli could explain alcohol's adverse effects on driving.

Many investigators have attempted to detect whether AERs in alcoholics differ from those in nonalcoholics. A frequently cited study demonstrated that, compared with nonalcoholics, alcoholics produce higher amplitude AERs when presented with light flashes of low intensity, even though these alcoholics had been abstinent from alcohol for 1 week or more (Buchsbaum and Ludwig 1980). When the flash intensity was increased, alcoholics' responses increased more than those of normal subjects. Thus, the alcoholics' AERs were somewhat greater than normals' at low intensities, but much greater at high intensities. Buchsbaum and Ludwig (1980) noted that alcoholics, in increasing their AERs at higher light intensities, are more sensitive to higher level stimuli. They speculated that alcoholics may be neurophysiologically vulnerable to intense sensory inputs either by predisposition or as a result of the toxic effects of alcohol, and that perhaps they use alcohol to diminish their augmented sensitivity.

One provocative question is whether differences seen in the AER are consequent to, or predispose for, alcoholism. Recent research indicates that there may be inherited differences in the brain's electrical activity. Elmasian et al. (1982) observed that AERs from groups of individuals with and without a family history of alcoholism were markedly different. These differences were apparent whether or not the individuals had consumed alcohol. Electrophysiological methods may, therefore, prove to be valuable in future research, especially in identifying specific indicators or markers of alcohol susceptibility.

Neural and Biochemical Effects

Behavior and thought, learning and memory, sensations and movements, all of which are affected by drinking alcohol, find their biological basis in the nervous system. The individual units of this system are neurons (nerve cells).

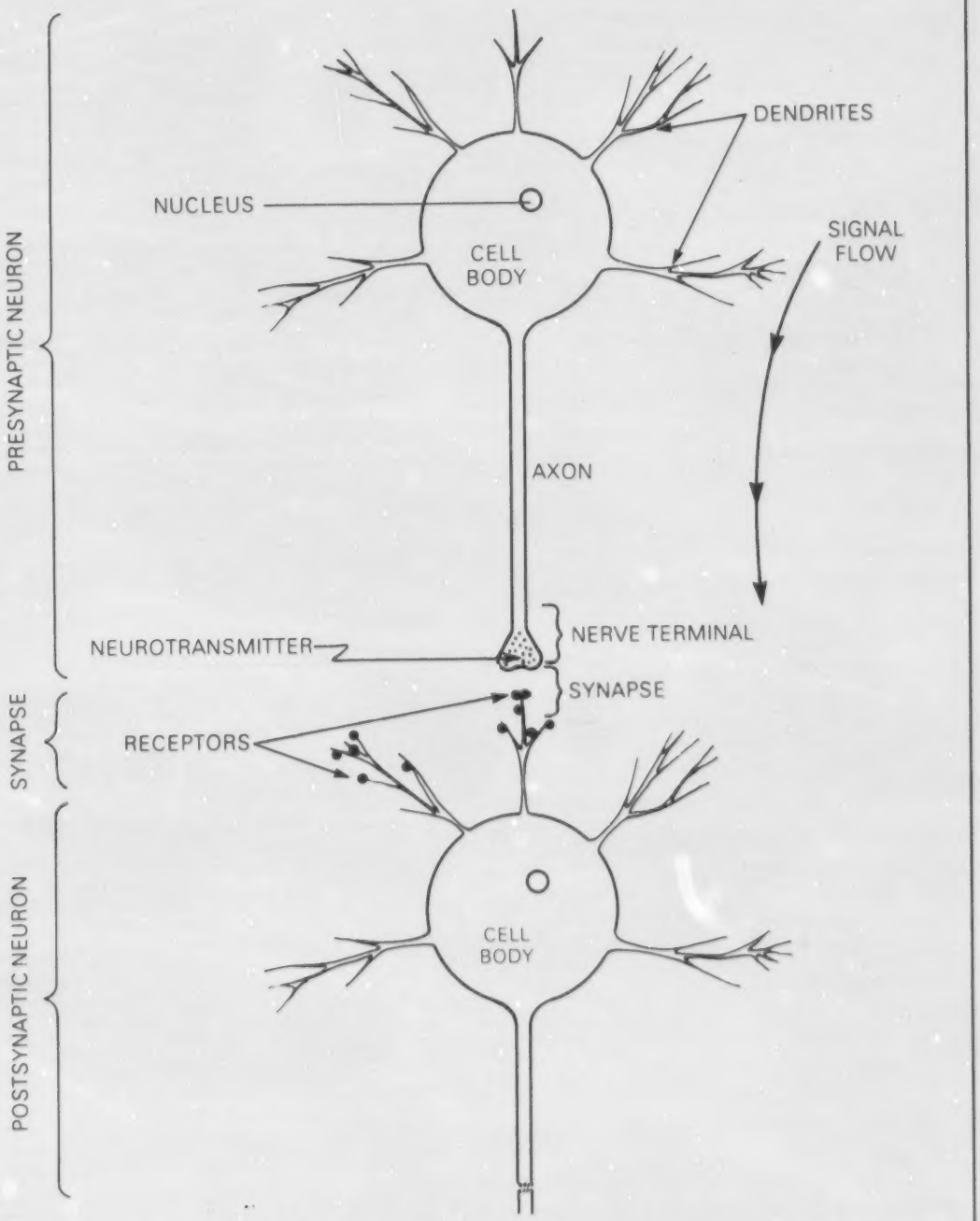
Neurons are now known to be extraordinarily subtle electrochemical processors. New knowledge of neurons, accompanied by new measurement techniques, has encouraged some optimism that a deeper examination of alcohol's effects on neurons could reveal how alcohol affects the nervous system and, in turn, how the nervous system affects behavior. Before discussing alcohol's effects on neurons, it is necessary to understand what a neuron is and how it works.

Neurons are, in computer parlance, logic elements. They conduct information and, based on a combination of electrical and chemical signals, communicate with other neurons, with muscles, and with the body's endocrine system hormones.

A typical neuron (shown highly simplified in figure 1) usually receives chemical inputs, through its dendrites, from other neurons. It changes the chemical signal into an electrical signal, which travels to the other end of the neuron (the nerve terminal or output end) where neurotransmitter chemicals, which continue to carry the signal, are released across a space called the synapse to adjacent neurons. The process is usually repeated many times to create signal paths throughout the nervous system. Essentially, the transmission between neurons is chemical, while the transmission within neurons is electrical.

If we probe into the nature of the electrical signal that is carried along the neuron, we find that it is formed by the movement of sodium and potassium ions (charged particles) flowing across the thin semipermeable membrane enclosing each nerve cell and crossing back again. When the flow of these ions reaches threshold conditions, an impulse is propagated down the neuron to its destination, the nerve terminal. Instruments can detect these short electrical pulses as the electrical signal travels through each neuron. Alcohol could affect the propagation of electrical pulses by making the membrane more or less permeable

Figure 1. Typical Nerve Cell (Neuron)



to the charged particles. After a pulse is propagated, the neuron must be recharged before it can carry another electrical impulse. This process is regulated by an enzyme that moves ions that entered the neuron back outside. Alcohol may also interfere with this ion "pump" mechanism, which maintains the electrical stability of each neuron.

When the electrical impulses reach the nerve terminal, calcium ions, acting as gatekeepers of the synaptic membrane, enter the neuron and allow tiny packets of neurotransmitter chemicals to be released across the synapse. On the adjacent neuron, receptors exquisitely matched to the neurotransmitter chemical characteristics will recognize the chemical message and unlock the membrane of the receiving neuron to allow the signal to continue. Continuation of the signal, inside the receiving neuron, depends on increased flow of sodium and potassium ions to reach the threshold conditions for generating an electrical impulse and allowing the whole process to repeat. (Depending on the neurotransmitter chemical, however, the receiving neuron may be inhibited from firing, rather than being fired. In this manner, the nervous system can turn off, as well as turn on, the flow of information.) This activity can occur hundreds of times a second and in billions of neurons in the brain. The result is thoughts, feelings, learning, or the link between a red light and muscles flexing to step on the brake. Any interference with the neurotransmission process could affect that link.

Electrical Conduction

In the late 1940s, it was found that sodium and potassium ions were responsible for the electrical conduction in the neuron. Researchers interested in alcohol's effect on the brain hypothesized that alcohol could impede the movement of ions necessary to produce and conduct the electrical impulse. Early studies on the squid's giant axon confirmed the hypothesis, but only at alcohol levels four to five times the lethal concentration (Gallego 1948). Therefore, many researchers concluded that alcohol's ionic effects could not explain why or how drinking alcohol could affect the nervous system. The hypothesis seemed to lead to a dead end. With time, new technology and instrumentation have allowed a more detailed view of the brain and individual neurons. After examining and recording the electrochemical activity of neurons throughout the brains of various mammals, it was found that a neuron is not simply a standard element repeated billions of times in the brain. Rather, a wide diversity exists among neurons--in speed of conduction, size, number of inputs, and chemical makeup; therefore, the case for alcohol's effect on neurons' electrical activity was reopened. It was realized that a differential sensitivity to alcohol might result because of differences between neurons.

Recently, researchers (Carlen et al. 1982; Shefner et al. 1982) have demonstrated that alcohol diminishes electrical activity in parts of the brain of mice and rats. In particular, neurons in the hippocampus and locus ceruieus, deep inside the brain, are affected by alcohol concentrations below those that might be expected in a person after several cocktails.

The differential sensitivity of various brain areas to alcohol seems to be genetically influenced. In a line of mice (LS) bred for sensitivity to the effects of alcohol, the hippocampus was less sensitive than another brain area, the cerebellum. These two brain areas were equally sensitive, however, to the effects of alcohol in another line of mice (SS), bred for resistance to alcohol's effects (Sorenson et al. 1981; Basile et al. 1982). Comparisons between strains also clearly demonstrated a genetically influenced differential response to alcohol. Neurons in the cerebellum of the mice resistant to the disruptive effect of alcohol were less affected electrophysiologically by alcohol (Sorenson et al. 1980, 1981; Basile et al. 1982) than were those from the sensitive mice.

The nature of the effects of alcohol on electrical activity led Carlen and his coworkers (1982) to postulate that alcohol altered, in a complex way, the movement of potassium ions across the neuronal membrane.

Another neuronal component related to the electrical activity of the cells is the enzyme sodium-potassium-ATPase. This enzyme, the ion "pump," is responsible for maintaining the proper concentrations of sodium and potassium ions on either side of the neuronal membrane. Alcohol alone in nonlethal amounts does not affect the enzyme activity. When combined with the neurotransmitter chemical norepinephrine, however, brain alcohol concentrations that could be achieved by beverage consumption can inhibit the enzyme. Such inhibition would be expected to affect the conduction of electrical impulses (Rangaraj and Kalant 1979). Thus, alcohol's effects on the locus ceruleus, which has norepinephrine-containing neurons, could be related to inhibition of the enzyme.

As mice and rats become more tolerant to the sedative effect of alcohol, the sodium-potassium-ATPase becomes more resistant to alcohol's inhibitory effects (Levental and Tabakoff 1980; Rangaraj and Kalant 1982). Such a change suggests that alcohol tolerance may, in part, be based on neurochemical changes in the brain. Clearly, more information is required to establish unequivocally the link between alcohol, electrical activity in the brain, and behavioral responses to alcohol.

Neurotransmission

Chemical messages carried across the synapses--the tiny spaces between adjacent neurons--are critical to brain function. Any interference with the release of neurotransmitters, their recognition by receptors, or the development of the new signal in the adjacent neuron will affect the flow of information in the brain. Without chemical transmission, brain function stops. Therefore, various researchers have examined the chemical flow at the synapse to determine the potential effects of alcohol on neuronal activity. Measurement of neurotransmitter release and metabolism represents an alternative to direct measurement of electrical activity, since the rate of neurotransmitter release and synthesis usually reflects the electrical activity of neurons.

The release and recognition of chemical neurotransmitters between neurons propagates messages through the brain. Neurochemicals are allowed to pass through the nerve cell membrane by a mechanism that is dependent on the movement of calcium ions into the neuron. Could alcohol interfere with this process? Friedman et al. (1980) found that alcohol stimulated the initial rate of calcium accumulation in a special preparation of neuronal membranes deprived of calcium. In another study on mice (Harris and Hood 1980), alcohol inhibited the flow of calcium into a neuronal membrane preparation that was enriched with calcium. Furthermore, this latter effect was detectable only under conditions that mimic the electrical signals' arrival at the synapse. In effect, when there was a message and no calcium ions, alcohol quickly mobilized a new calcium cadre. With an excess of calcium ions, however, alcohol inhibited the calcium stimulated release of neurotransmitter.

Recent studies (Stokes and Harris 1982) have found that the inhibitory effects of alcohol on calcium uptake depend on the part of the brain that is examined. Samples from rat striatum and cerebellum (both associated with movement) were more sensitive to alcohol's effects than were samples from the cortex and brain stem. These results confirm again that, even at the chemical level, different brain areas seem to respond according to their own programs.

Perhaps more important, neuronal preparations from mice chronically fed alcohol resisted alcohol's effects on calcium uptake, regardless of what the initial alcohol effects were. This evidence suggests a possible direct link between behavioral tolerance of alcohol and the microenvironment of the neuron.

The aforementioned studies measured alcohol's effects on the uptake of calcium--that is, the movement of calcium ions into the neuron. Calcium is also stored within cells near the membrane in a kind of chemically adhesive process called binding, which is also affected by alcohol. Low levels of alcohol increased the binding of calcium, whereas higher levels were not as effective (Michaelis and Myers 1979). As with calcium uptake, alcohol had little effect on calcium binding when added to neuronal preparations from rats fed a chronic diet containing alcohol. Thus, this study also indicates a link between behavioral and biochemical tolerance. It is, however, premature to conclude that behavioral tolerance is the direct result of alcohol's effects on calcium--whether related to calcium uptake or binding.

Evidence linking neurotransmitters to behavior led alcohol researchers to investigate three neurotransmitter systems: norepinephrine, dopamine, and GABA (gamma-aminobutyric acid). They found that alcohol affects the release of the neurotransmitters as well as their recognition by receptors at the postsynaptic membrane (Bacoupoulos et al. 1978; Ticku and Burch 1980; Rabin et al. 1980).

When alcohol is acutely given to an animal, the amount of norepinephrine released depends on the level of alcohol in the brain. Moreover, the process is biphasic: It reverses with larger amounts of alcohol (Hunt and Majchrowicz 1974). That is, a small amount of alcohol leads to an increased release of norepinephrine, while higher doses actually depress the release of norepinephrine. Since release of a neurotransmitter reflects nerve activity, this suggests that low doses of alcohol have an excitant or disinhibiting effect, while high doses have an inhibiting effect on neurons containing norepinephrine. These effects on norepinephrine release may, in turn, be related to the behavioral changes produced by alcohol. Sim-

ilar results were obtained when the effects of alcohol on dopamine were examined in rats (Hunt 1981). In mice, however, the reaction is reversed (Kiianmaa and Tabakoff 1983). Low doses of alcohol lead to low release of dopamine, whereas higher doses lead to greater release. The causes of these different reactions to acute infusions of alcohol in closely related species are not yet understood; they may, however, be related to different organization of the nervous system of these species. In both species, the effect of chronic doses of alcohol is consistent, leading to increased release of norepinephrine and decreased release of dopamine (Hunt and Majchrowicz 1974; Pohorecky 1974).

Over the years, laboratory animals have been bred with specific characteristics in mind. One strain of mice has been developed for its relatively high resistance to the behavioral effects of alcohol. These mice are also more resistant to the effects of alcohol on dopamine release (Kiianmaa and Tabakoff 1983). This finding suggests that some animals may be genetically more tolerant of alcohol than others, and that differences in behavior may be related to differences in biochemistry.

The preceding research collectively shows that alcohol's effects on norepinephrine and dopamine release, as well as on movement of calcium ions, vary with dosage, species, genetic strain, and brain area.

The discussion thus far has focused on the neurotransmitters at the transmitting neuron. Across the synapse, the receiving neuron with its receptors must recognize the neurotransmitters. Much of the research at the receptor end has been devoted to GABA, a neurotransmitter that inhibits firing in neurons and is of particular interest to alcohol researchers. By inhibiting electrical impulses, it controls the tendency to convulsions, which are caused by uncontrolled electrochemical activity in the brain. Because the symptoms of alcohol withdrawal include convulsions, GABA is a prime suspect as a cause of these symptoms.

In fact, research strongly implicates GABA receptors in alcohol withdrawal symptoms. In mice, an acute dose of alcohol results in an increase in the number of GABA receptor sites (Ticku and Burch 1980), suggesting lessened neural activity. This finding is consistent with alcohol's depressive effects. Chronic administration of alcohol results, conversely, in a decrease in the number of GABA receptor sites--a finding that could explain convulsions in withdrawals. Indeed, in rats, the decreased number of receptor sites was most pronounced at the time of the most severe withdrawal symptoms.

Clinical results demonstrate that benzodiazepines such as diazepam (Valium^{R}) and chlordiazepoxide (Librium^{R}) control the major symptoms (especially convulsions) of alcohol withdrawal. Specific receptors in the nervous system for the benzodiazepines are related to GABA receptors. Part of this relationship appears to be a common effect on the flow of chloride ions across the nerve membrane. It appears that alcohol disturbs the natural linkage between GABA and diazepam. The strongest evidence for this effect comes from studies in which the receptors were removed from their normal membrane environment (Ticku and Burch 1980).

Recent studies have demonstrated that chronic feeding of alcohol to animals affects the receptors for other neurochemical messengers, including the endogenous opiates (Hoffman et al. 1982), acetylcholine (Tabakoff et al. 1979), norepinephrine (Rabin et al. 1980), and dopamine (Barbaccia et al. 1982).

After the receptors have recognized the neurotransmitter message, a new signal is generated within the receiving neuron. A chemical (cyclic adenosinemonophosphate or cAMP) sometimes called the second messenger carries the message from the receptors to the interior of the receiving neuron. Recent research indicates that after withdrawal of animals from chronic alcohol treatment, the release of the second messenger is inhibited (Tabakoff and Hoffman 1979; Luthin et al. 1983).

As the number of identified neurotransmitters increases (some researchers expect it to go from the current 40 to as many as 200 or even more), and with growth in understanding how they work, neurotransmission is likely to help explain the nature of alcohol's biological effects on the central nervous system.

The Membrane

The transmission of information between nerve cells is dependent upon the function of receptors, enzymes, and ion gates. All of these components are proteins located in and on the neuronal membrane. Changes in the physical state of these membranes could have adverse effects on the ability of the specialized proteins to function normally. A number of researchers are studying this problem and in particular are examining the lipids in membranes, which are the biochemically important elements in maintaining the structural integ-

rity of the membrane. Results have clearly shown that membrane viscosity is decreased by acute treatment with levels of alcohol that can be attained through consumption of alcoholic beverages (Chin and Goldstein 1977). After chronic treatment of mice with alcohol, however, it was found that subsequent acute doses of alcohol would no longer change the viscosity of neuronal membranes (Chin and Goldstein 1977). This suggests that behavioral tolerance to alcohol may, in part, be associated with a tolerance of membrane lipids to alcohol-induced decrease in viscosity.

Goldstein et al. (1982) compared alcohol's effects on neuronal membranes from two different genetic strains of mice: LS mice (long sleep, with greater sensitivity to alcohol) and SS mice (short sleep, with less sensitivity to alcohol). They found that neuronal membranes taken from LS mice were more sensitive to alcohol than were membranes taken from SS mice. Another study (Lyon et al. 1981) showed that alcohol's well-known sedative effect is correlated with its effects on neuronal membranes. In turn, these membrane effects would be expected to influence the function of the specialized proteins that reside in the membrane and are critical for proper neuronal transmission.

Tolerance and Dependence

Alcohol produces tolerance in chronic drinkers--that is, the subjective effects of alcohol decrease with continued exposure. It may take a chronic drinker a pint of whisky to obtain the same effect that an occasional drinker gets with a cocktail or two. Physical dependence--the need to continue to drink alcohol to prevent withdrawal symptoms--may be related to tolerance, as it develops only after chronic ingestion of alcohol.

At one time, it was thought that tolerance and dependence would develop only after relatively long periods of exposure. A recent study (Gallaher et al. 1982), however, found that tolerance to alcohol's ataxic effects (loss of muscular coordination) developed after only 2 days. The fairly straightforward behavioral effects of tolerance and dependence have yet to be described fully; biological mechanisms underlying these phenomena are currently even more obscure.

Recent studies suggest that learning may play an important role in developing tolerance, and several investigators have proposed a Pavlovian model of alcohol tolerance (Crowell et al. 1981; Melchior and Tabakoff 1981). According to this model, animals learn to associate environmental cues with the pharmacological effect of alcohol, much as Pavlov's famous dog associated a bell with food. In the presence of those cues, an animal may develop a response designed to counteract the effect of alcohol. In essence, the Pavlovian model suggests that animals learn to reduce their response to alcohol in a particular context, which provides the cues for their response. Tolerance is reduced or absent, however, when the animal is subsequently tested in a different environment. Thus, in some cases, the mere exposure of an animal to alcohol is not sufficient to cause tolerance development; the initial environmental cues must be repeated (Crowell et al. 1981).

Neurochemical studies have also suggested that the presence of alcohol, while necessary, is not a sufficient condition for the development of tolerance; neurons containing the neurotransmitters norepinephrine and serotonin seem to play a role in developing tolerance. When those neurons were destroyed, animals tended to retain their initial responses to alcohol (Tabakoff and Ritzmann 1977; Le et al. 1981) or to develop tolerance more slowly. Thus, the activity of specific neuronal systems, in conjunction with alcohol, seems to be quite important for tolerance development. In addition to neurotransmitter systems, certain hormonal systems appear to affect the development of tolerance. Vasopressin (sometimes called antidiuretic hormone) can maintain an already developed tolerance, even in the absence of continued exposure of the organism to alcohol (Hoffman et al. 1978). Vasopressin's ability to maintain tolerance depends on the presence of intact norepinephrine--and/or serotonin-containing neuronal pathways (Le et al. 1982; Hoffman et al. in press). Whether vasopressin plays a role in developing alcohol tolerance under normal conditions is not clear, but in at least one study, a strain of rats lacking this hormone could not develop alcohol tolerance (Pittman et al. 1982).

Changes in neuronal membranes could account for tolerance and physical dependence. Alcohol initially increases membrane fluidity, but membranes from alcohol-tolerant animals are less sensitive to this effect. Also, enzymes in the membrane demonstrate a biochemical tolerance to alcohol (Levental and Tabakoff 1980; Rangaraj and Kalant 1982). Membrane fluidity could affect sodium-potassium-ATPase activity and therefore, indirectly, electrical conduction in the brain. The mem-

brane's biochemical adaptation could be related to behavioral tolerance.

Physical dependence, like tolerance, may result from an adaptation of neuronal membranes during chronic alcohol exposure. This adaptation might be expected to produce inappropriate neuronal activity in the absence of alcohol. If so, when alcohol is withdrawn, the membranes of physically dependent animals might be more viscous than normal. Although initial studies did not reveal such changes in animals' brain cell membranes following chronic alcohol consumption (Chin and Goldstein 1977), more recent studies have confirmed the expectations (Lyon and Goldstein 1983). Another study (Ingram 1982) also cataloged a number of changes in lipid (fat) content of brain cell membranes derived from chronically alcohol-fed animals, which could contribute to changes in fluidity. These adaptive changes could well be responsible for some aspects of physical dependence and tolerance.

Tolerance and dependence are complex phenomena, however, and may result from different but interacting biochemical mechanisms. As tolerance and dependence are studied in more detail, it becomes increasingly clear that they are influenced by various neuronal and hormonal systems.

Theories of Alcohol's Effects

Alcohol as Reinforcer

Since the publication of the Fourth Special Report (USDHHS 1981), a new hypothesis has emerged to explain the mechanism behind alcohol's reinforcing activity. Most earlier studies focused on specific neurochemical and behavioral correlates of alcohol's depressive effects. Although the stimulant effects had been noted in the past (USDHEW 1974, 1978; Hunt and Overstreet 1977; USDHHS 1981), most earlier studies lacked the theoretical focus that has emerged in recent years. Now much of alcohol's appeal is thought to be directly related to its excitatory effects, and many current studies are attempting to verify the relationship (Taberner 1980; Lindman 1982).

Essentially all studies of alcohol as a drug of abuse are based on the premise that humans and animals consume alcohol because of its reinforcing (or rewarding) effects. Recent years have seen considerable interest in the similarities between alcohol's reinforcing properties and those of other drugs of abuse. But how does reinforcement work? Many researchers have noted the similarity between the reinforcing properties of alcohol and those of opiate drugs (Altshuler 1982; Amit and Brown 1982). They have reasoned, therefore, that drugs (opiate antagonists) that nullify the brain's reaction to opiates may well block similar reactions to alcohol. The research results have been somewhat difficult to interpret. In some cases, the opiate antagonist blocked a specific effect of alcohol, while in others the opiate antagonist was ineffective.

Striking similarities have been reported between the electrophysiological effects of alcohol and opiates, especially opiate peptides naturally occurring in mammals (Siggins and Bloom 1980; Siggins et al. 1982; Hoffman et al. 1982). Furthermore, in rats and mice, chronic alcohol doses caused significant changes in the characteristics of opiate receptors (Hoffman et al. 1982). All of these reports confirm the link between alcohol and the opiate system in the central nervous system. In general, it appears that, while opiate antagonists do not affect alcohol's depressive properties, they can alter some of its stimulant or excitatory properties.

Such findings suggest a possible relationship between alcohol's excitatory effects and the phenomenon known as reinforcement. Drinking studies conducted with almost every laboratory species have provided many demonstrations that alcohol is a reinforcer in animals as it is in humans.

Some researchers contend that the most appropriate way to study alcohol reinforcement in laboratory animals is to study their voluntary oral alcohol consumption. Yet the usefulness of oral alcohol consumption studies in animals for measuring alcohol preference or reinforcement has been a persistent source of disagreement among researchers. Advocates contend that since humans consume alcohol by drinking it, oral studies are most likely to provide meaningful results. Opponents argue that when drugs, including alcohol, are taken orally, animals will choose them based on flavor rather than for their reinforcing effects. The problem of estimating or controlling how flavor affects oral intake studies has plagued researchers for many years, but a recent study (Crawford and Baker 1982) suggests a method to distinguish between the reinforcing effects of flavor and alcohol.

Because drinking studies in animals are often difficult to conduct, a technique called

self-administration was developed to substitute for oral consumption. The technique allows animals to work for alcohol by pressing a lever to obtain intravenous (directly into a vein) or intragastric (into the stomach) alcohol infusions through surgically implanted cannulae (tubes). Early studies (Deneau et al. 1969) demonstrated unequivocally that monkeys would self-administer alcohol intravenously. Altshuler (1982) showed that monkeys would also self-administer alcohol intragastrically for extended time periods. Both investigations showed that many animals would work for alcohol over time periods sufficiently long to develop tolerance, physical dependence, and eventually, alcohol-related toxicity.

Another less direct technique to measure alcohol's reinforcing effects is the intracranial self-stimulation (ICSS) model. Stimulating electrodes are placed in parts of the brain where electrical stimulation presumably produces pleasurable sensations. The animals, usually rats, are able to press a lever to activate the stimulating electrode in their brains. Most animals will press the lever frequently to obtain the apparently pleasurable sensation that follows. This ICSS phenomenon is thought to be associated with many different reinforcers, perhaps through a common pathway or center of reinforcement. Indeed, most addictive drugs seem to affect ICSS. Because alcohol (and other reinforcing drugs) changes the rate at which animals will press the lever during ICSS, a number of researchers (Wise 1980; Amit and Brown 1982) have concluded that the drugs were acting as reinforcers.

A controversy has emerged over the neurochemical mechanism responsible for alcohol's reinforcing properties in the ICSS model. Most researchers agree that alcohol is a reinforcer and that reinforcement is controlled by the brain's reward system (Wise 1980; Amit and Brown 1982). Wise (1980) hypothesized that alcohol affects dopamine's role in information transfer within the reward system. Amit and Brown (1982) suggested that norepinephrine rather than dopamine is affected. In either event, alcohol reinforcement is probably associated with a specific cluster of neurons that may also be the site of the reinforcement produced by several drugs and ICSS. The experimental evidence implicates several neurotransmitters, including dopamine, norepinephrine, and opiate peptides, as the neurochemicals responsible for the reinforcing properties of alcohol.

Alcohol Metabolism and TIQs

Another theory about alcohol and its actions is based on the hypothesis that biologically active chemicals called tetrahydroisoquinolines (TIQs) may be formed during alcohol metabolism (Davis and Walsh 1970). Interest arose in these compounds because some of the TIQs are structurally related to morphine (an opiate) and, therefore, could involve a common addictive mechanism.

About 6 years ago, Myers and Melchior (1977) proposed a provocative hypothesis relating TIQs and alcoholism. The hypothesis was based on the observation that infusions of a TIQ, tetrahydropapaveroline (THP), into a brain cavity changed an animal's drinking behavior from rejecting alcohol to choosing moderate doses. It was speculated that excessive drinking by human alcoholics could be caused by metabolic abnormalities that result in the formation of TIQs. They reasoned that because drinking creates TIQs, and TIQs stimulate drinking, the positive feedback loop could explain uncontrolled drinking by alcoholics. That conjecture generated both support and disagreement, which continue unabated to this day. Several research groups (Sinclair et al. 1982; Tuomisto et al. 1982) attempted to replicate the initial studies with, at best, only mixed results. Myers et al. (1982), however, reported recently that TIQ infusions produced outcomes in monkeys identical to those in rats, and that THP infusions produced increased alcohol drinking by monkeys. However, these infusion studies use TIQ that is synthesized in the laboratory. While it is theoretically possible that TIQ is formed in the brain, a great deal of controversy remains as to whether TIQs are in fact formed in the brain, or if the concentrations of these chemical compounds are increased following alcohol ingestion. A number of investigators have searched for these compounds using increasingly sophisticated and sensitive techniques, with only limited success (Bloom et al. 1982).

A less controversial hypothesis relates endogenous (naturally produced in the brain) opiate mechanisms to alcohol's behavioral effects. These studies have investigated possible pharmacological relationships between TIQs, endogenous opiate compounds, and the reinforcing properties of alcohol. Most have reported that the reinforcing properties of alcohol and opiates could be related to TIQ mechanisms.

In future studies, many researchers will probably turn their attention to the biphasic effects of alcohol and may reexamine many assumptions about its effects on behavior. Additional research about alcohol reinforcement, preference, and voluntary consumption is likely to illuminate the role of the TIQs, opiate mechanisms, and alcohol-induced stimulation. These data may provide an understanding of the underlying biological mechanisms that contribute to alcohol abuse.

Summary

Alcohol affects every level of the nervous system--from the neurochemicals within single cells to the macrofunctions governing thought processes and behavior. Research on cognition and brain responses to various stimuli continues to expand the inventory of alcohol's effects on humans. Driving-related studies have shown that alcohol impairs judgment, attention, information processing, and reaction time. Alcohol also alters the brain's responses to visual and auditory stimuli. Chronic drinking affects memory and the ability to detect small differences and creates such autonomic difficulties as lack of proper eye pupil control. Abstinence can reverse alcohol's cognitive effects more easily in young drinkers than in older ones.

Social drinking appears to result in some cognitive impairment, but methodologic issues cloud the picture. Alcoholism, on the other hand, definitely impairs cognitive performance. Late stages of alcoholism may also result in organic brain damage--alcoholic dementia and Korsakoff's psychosis.

Alcohol may be the indirect cause of other neuropathology. Liver damage, head trauma, malnutrition, and breathing impairment during sleep, resulting from alcoholism, can lead to a range of adverse effects from behavioral deficits to serious brain damage.

In an effort to understand the neuropsychological effects of alcohol, researchers have examined the effects of alcohol on structures and neurochemicals in various regions of the brain. Chronic drinking seems to cause several biochemical adaptations in nerve cells that could partially explain why alcoholics become tolerant to alcohol and why they suffer withdrawal symptoms after sudden abstinence.

In a search to explain why people drink alcohol to excess, researchers have proposed several theories. One theory suggests that alcohol's appeal stems from its initial excitatory effects. Animal research tends to support the theory, as animals will work to receive infusions of alcohol--thus meeting one criterion of reinforcement.

Another provocative preliminary hypothesis is that tetrahydroisoquinolines, or TIQs, may play a role in habitual heavy drinking. TIQs are formed when alcohol is metabolized. In some animal experiments, when these chemicals are injected into the brains of previously abstinent animals preference for alcohol is increased.

Empirical and theoretical progress over the past decade offers encouragement that research will continue to acquire fundamental knowledge essential to understanding how humans react to alcohol and what makes them drink excessively.

References

Adams, K.M.; Grant, I.; and Reed, R. Neuropsychology in alcoholic men in their late thirties: One-year follow-up. American Journal of Psychiatry 137:928-931, 1980.

Alling, C., and Bostrom, K. Demyelination of the mamillary bodies in alcoholism. Acta Neuropathologica (Berlin) 50:77-80, 1980.

Altshuler, H.L. Ethanol reinforcement: Self-administration and discriminative stimulus parameters. In: Saito, S., and Yanagita, T., eds. Learning and Memory: Drugs as Reinforcer. Proceedings of symposiums on the Pharmacology of Learning and Memory and on Drugs as Reinforcers (1981). Amsterdam: Excerpta Medica, 1982. pp. 240-256.

Amit, Z., and Brown, Z.W. Actions of drugs of abuse on brain reward systems: A reconsideration with specific attention to alcohol. Pharmacology, Biochemistry and Behavior 17:233-238, 1982.

Andreasen, N.C., and Winokur, G. Secondary depression: Familial, clinical, and research perspective. American Journal of Psychiatry 136: 62-66, 1979.

Bacopoulos, N.G.; Bhatanger, R.K.; and van Orden, L.S. The effects of subhypnotic doses of ethanol on regional catecholamine turnover. Journal of Pharmacology and Experimental Therapeutics 204:1-10, 1978.

Ballenger, J.C.; Goodwin, F.K.; Major, L.F.; and Brown, G.L. Alcohol and central serotonin metabolism in man. Archives of General Psychiatry 36:224-227, 1979.

Barbaccia, M.L.; Bosio, A.; Lucchi, L.; Spano, P.F.; and Trabucchi, M. Neuronal mechanisms regulating ethanol effects on the dopaminergic sys-

tem. Life Sciences 30:2163-2170, 1982.

Basile, A.S.; Dunwiddie, T.V.; and Hoffer, B.J. Ethanol effects on Purkinje cell spontaneous activity in the in vitro cerebellum of mice differentially sensitive to ethanol (abstract). Federation Proceedings 41:1465 (A.6983), 1982.

Behar, D., and Winokur, G. Research in alcoholism and depression: A two-way street under construction. In: Pickens, R.W., and Heston, L.L., eds. Psychiatric Factors in Drug Abuse. New York: Grune & Stratton, 1979. pp. 125-152.

Blass, J.P. Metabolic dementia. In: Amaducci et al., eds. Aging of the Brain and Dementia. Vol. 13. Aging. New York: Raven Press, 1980. pp. 261-270.

Bloom, S.; Barchas, J.; Sandler, M.; and Usdin, E., eds. Beta-Carbolines and Tetrahydroisoquinolines. Progress in Clinical and Biological Research, Vol. 90. New York: Alan R. Liss, 1982.

Brown, G.L.; Ebert, M.H.; Goyer, P.F.; Jimerson, D.C.; Klein, W.J.; Bunney, W.E.; and Goodwin, F.K. Aggression, suicide, and serotonin: Relationship to CSF amine metabolites. American Journal of Psychiatry 139:741-746, 1982.

Buchsbaum, M.S., and Ludwig, A.M. Effects of sensory input and alcohol administration on visual evoked potentials in normal subjects and alcoholics. In: Begleiter, H., ed. Biological Effects of Alcohol: Advances in Experimental Medicine and Biology. Vol. 126. New York: Plenum Press, 1980. pp. 561-571.

Butters, N. The Wernicke-Korsakoff syndrome. In: National Institute on Alcohol Abuse and Alcoholism. Biomedical Processes and Consequences of Alcohol Use. Alcohol and Health Monograph No. 2. DHHS Pub. No. (ADM) 82-1191. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 257-287.

Carlen, P.L.; Gurevich, N.; and Durand, D. Ethanol in low doses augments calcium-mediated mechanisms measured intracellularly in hippocampal neurons. Science 215:306-309, 1982.

Carlen, P.L.; Lee, M.A.; Jacob, M.; and Livshits, O. Parkinsonism provoked by alcoholism. Annals of Neurology 9:84-86, 1981a.

Carlen, P.L.; Wilkinson, D.A.; Wortzman, G., Holgate, R.; Cordingley, J.; Lee, M.A.; Huszar, L.; Moddel, G.; Singh, R.; Kiraly, L.; and Rankin, J.G. Cerebral atrophy and functional deficits in alcoholics without clinically apparent liver disease. Neurology (New York) 31:377-385, 1981b.

Chaney, E.F.; O'Leary, M.R.; Fehrenbach, P.A.; and Donovan, D. Cognitive deficit in middle-aged alcoholics. Drug and Alcohol Dependence 6(4):219-226, 1980.

Chin, J.H., and Goldstein, D.B. Effects of low concentrations of ethanol on the fluidity of spin-labeled erythrocyte and brain membranes. Molecular Pharmacology 13:435-441, 1977.

Clayton, A.B. Effects of alcohol on driving skills. In: Sandler, M., ed. Psychopharmacology of Alcohol. New York: Raven Press, 1980. pp. 73-78.

Colins, W.E., and Chiles, W.D. Laboratory performance during acute alcohol intoxication and hangover. Human Factors 22:445-462, 1980.

Coppen, A. Lithium in the treatment of alcoholism. In: Sandler, M., ed. Psychopharmacology of Alcohol. New York: Raven Press, 1980. pp. 209-214.

Cravioto, H.; Korein, J.; and Silberman, J. Wernicke's encephalopathy. A clinical and pathological study of 28 autopsied cases. Archives of Neurology 4:510-519, 1961.

Crawford, D., and Baker, T.B. Alcohol dependence and taste-mediated learning in the rat. Pharmacology, Biochemistry and Behavior 16:253-261, 1982.

Crowell, C.R.; Hinson, R.E.; and Siegel, S. The role of conditioned drug responses in tolerance to the hypothermic effects of ethanol. Psychopharmacology 73:51-54, 1981.

Cutting, J. The relationship between Korsakov's syndrome and "alcoholic dementia." British Journal of Psychiatry 132:240-251, 1978.

Davis, V.E., and Walsh, M.J. Alcohol, amines and alkaloids: A possible biochemical basis of alcohol addiction. Science 167:1005-1007, 1970.

Deneau, G.; Yanagita, T.; and Seevers, M.H. Self-administration of psychoactive substances by the monkey: A measure of psychological dependence. Psychopharmacologia 16:30-48, 1969.

Eckardt, M.J.; Parker, E.S.; Pautler, C.P.; Noble, E.P.; and Gottschalk, L.A. Neuropsychological consequences of posttreatment drinking behavior in male alcoholics. Psychiatry Research 2:135-147, 1980.

Eckert, E.D.; Goldberg, S.C.; Halmi, K.A.; Casper, R.C.; and Davis, J.M. Alcoholism in anorexia nervosa. In: Pickens, R.W., and Heston, L.L., eds. Psychiatric Factors in Drug Abuse. New York: Grune & Stratton, 1979. pp. 267-283.

Elmasian, R.; Neville, H.; Woods, D.; Schuckit, M.; and Bloom, F. Event-related brain potentials are different in individuals at high and low risk for developing alcoholism. Proceedings of the National Academy of Sciences 79:7900-7903, 1982.

Freund, G., and Butters, N. Alcohol and aging: Challenges for the future. Alcoholism: Clinical and Experimental Research 6:1-2, 1982.

Friedman, M.B.; Erickson, C.K.; and Leslie, S.W. Effects of acute and chronic ethanol administration on whole mouse brain synaptosomal calcium influx. Biochemical Pharmacology 29:1903-1908, 1980.

Gallaher, E.J.; Parsons, L.M.; and Goldstein, D.B. The rapid onset of tolerance to ataxic effects of ethanol in mice. Psychopharmacology 78:67-70, 1982.

Gallego, A. On the effect of ethyl alcohol upon frog nerve. Journal of Cellular Comparative Physiology 31:97-106, 1948.

Goldstein, D.B.; Chin, J.H.; and Lyon, R.C. Ethanol disordering of spin-labeled mouse brain membranes: Correlation with genetically determined ethanol sensitivity of mice. Proceedings of the National Academy of Sciences 79:4231- 4233, 1982.

Goodwin, D.W., and Guze, S.B. Psychiatric Diagnosis. 2d ed. New York: Oxford University Press, 1979. pp. 118-144.

64

Goodwin, D.W.; Schulsinger, F.; Hermansen, L.; Guse, S.B.; and Winokur, G. Alcoholism and the hyperactive child syndrome. Journal of Nervous and Mental Diseases 160:349-353, 1975.

Gottfries, C.G. Activity of monoamine oxidase and brain levels of monoamines in alcoholics. In: Richeter, D., ed. Addiction and Brain Damage. Baltimore: University Park Press, 1980. pp. 228-239.

Grupp, L.A. The influence of some neurotransmitter agonists and antagonists on the response of hippocampal units and the cortical EEG to ethanol in the awake rat. Psychopharmacology 75:327-334, 1981.

Guilleminault, C.; van den Hoed, J.; and Mitler, M.M. Clinical overview of the sleep apnea syndromes. In: Guilleminault, C., and Dement, W.C., eds. Sleep Apnea Syndromes. Kroc Research Series, Vol. 11. New York: A.R. Liss, 1978. pp. 1-12.

Hamm, J.E.; Major, L.F.; and Brown, G.L. The quantitative measurement of depression and anxiety in male alcoholics. American Journal of Psychiatry 136:580-582, 1979.

Harper, C. Wernicke's encephalopathy: A more common disease than realised: A neuropathological study of 51 cases. Journal of Neurology, Neurosurgery and Psychiatry 42:226-231, 1979.

Harper, C. Neuropathology of brain damage caused by alcohol. Medical Journal of Australia 2:277-282, 1982.

Harris, R.A., and Hood, W.F. Inhibition of synaptosomal calcium uptake by ethanol. Journal of Pharmacology and Experimental Therapeutics 213:562-568, 1980.

Hetzler, B.E.; Heilbronner, R.L.; Griffin, J.; and Griffin, G. Effects of ethanol on visual cortex and superior colliculus evoked potentials in rats (abstract). Drug and Alcohol Dependence 6:88-89, 1980.

Hillbom, M., and Kaste, M. Alcohol intoxication: A risk factor for primary subarachnoid hemorrhage. Neurology (New York) 32:706-711, 1982.

Hoffman, P.L.; Melchior, C.L.; and Tabakoff, B. Vasopressin maintenance of ethanol tolerance requires intact brain noradrenergic systems. Life Sciences, in press.

Hoffman, P.L.; Ritzmann, R.F.; Walter, R.; and Tabakoff, B. Arginine vasopressin maintains ethanol tolerance. Nature 276:614-616, 1978.

Hoffman, P.L.; Urwyler, S.; and Tabakoff, B. Alterations in opiate receptor function after chronic ethanol exposure. Journal of Pharmacology and Experimental Therapeutics 222:182-189, 1982.

Hoyumpa, A.M., Jr. Mechanisms of thiamin deficiency in chronic alcoholism. American Journal of Clinical Nutrition 33:2750-2761, 1980.

Hunt, G.P., and Overstreet, D.H. Evidence for parallel development of tolerance to the hyperactivating and discoordinating effects of ethanol. Psychopharmacology 55:75-81, 1977.

Hunt, W.A. Neurotransmitter function in the basal ganglia after acute and chronic ethanol treatment. Federation Proceedings 40:2077-2081, 1981.

Hunt, W.A., and Majchrowicz, E. Alterations in the turnover of brain norepinephrine and dopamine in alcohol-dependent rats. Journal of Neurochemistry 23:549-552, 1974.

Ingram, L.O. Effect of alcohol on membranes. In: National Institute on Alcohol Abuse and Alcoholism. Biomedical Processes and Consequences of Alcohol Use. Alcohol and Health Monograph No. 2. USDHHS Pub. No. (ADM)82-1191. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 3-27.

Kearsley, J.H., and Musso, A.F. Hypothermia and coma in the Wernicke-Korsakoff syndrome. Medical Journal of Australia 2:504-506, 1980.

Kilanmaa, K., and Tabakoff, B. Neurochemical correlates to tolerance and the biphasic behavioral effects of ethanol. Pharmacology, Biochemistry and Behavior 18 (Supplement 1): 383-388, 1983.

Klemm, W.R., and Sherry, C.J. Messages in the brain: "Scrambling" by alcohol (abstract). Alcoholism: Clinical and Experimental Research 5:158, 1981.

Le, A.D.; Kalant, H.; and Khanna, J.M. Interaction between des-Glycinamide^9-[Arg^8] vasopressin and serotonin on ethanol tolerance. European Journal of Pharmacology 80:337-345, 1982.

Le, A.D.; Khanna, J.M.; Kalant, H.; and LeBlanc, A.E. The effect of lesions in the dorsal, median and magnus raphe nuclei on the development of tolerance to ethanol. Journal of Pharmacology and Experimental Therapeutics 218:525-529, 1981.

Leigh, D.; McBurney, A.; and McIlwain, H. Erythrocyte transketolase activity in the Wernicke-Korsakoff syndrome. British Journal of Psychiatry 139:153-156, 1981.

Levental, M., and Tabakoff, B. Sodium-potassium-activated adenosine triphosphatase activity as a measure of neuronal membrane characteristics in ethanol-tolerant animals. Journal of Pharmacology and Experimental Therapeutics 212:315-319, 1980.

Lindman, R. Social and solitary drinking: Effects on consumption and mood in male social drinkers. Physiology and Behavior 28:1093-1095, 1982.

Linnoila, M., and Martin, P.R. Benzodiazepines and alcoholism. In: Trimble, M.R., ed. Benzodiazepines Divided. New York: John Wiley & Sons, 1982. pp. 291-308.

Lishman, W.A. Cerebral disorder in alcoholism: Syndromes of impairment. Brain 104:1-20, 1981.

Lyon, R.C., and Goldstein, D.B. Changes in synaptic membrane order associated with chronic ethanol treatment in mice. Molecular Pharmacology 23:86-91, 1983.

Lyon, R.C.; McComb, J.A.; Schreurs, J.; and Goldstein, D.B. A relationship between alcohol intoxication and the disordering of brain membranes by a series of short-chain alcohols. Journal of Pharmacology and Experimental Therapeutics 318:669-675, 1981.

MacVane, J.; Butters, N.; Montgomery, K.; and Farber, J. Cognitive functioning in men social drinkers. A replication study. Journal of Studies

on Alcohol 43:81-95, 1982.
Mair, R.G.; McEntee, W.J.; and Zatorre, R.J. Brain, NE and DA activity: correlation with specific behavioral deficits in Korsakoff's psychosis. Neurology (New York) 32:A66-67, 1982.
Martin, P.R. The human genetics of alcoholism. Substance and Alcohol Actions/Misuse 2:389-406, 1981.
McLeod, J.G. Alcohol, nutrition, and the nervous system. Medical Journal of Australia 2:273-274, 1982.
McNamee, J.E.; Tong, J.E.; and Piggins, D.J. Effects of alcohol on velocity perception: I. Stimulus velocity and change in performance over time. Perceptual and Motor Skill. 51:779-785, 1980.
Melchior, C.L., and Tabakoff, B. Modification of environmentally cued tolerance to ethanol in mice. Journal of Pharmacology and Experimental Therapeutics 219:175-180, 1981.
Michaelis, E.K., and Myers, S.L. Calcium binding to brain synaptosomes: Effects of chronic ethanol intake. Biochemical Pharmacology 28:2081-2087, 1979.
Moody, D.B.; Winger, G.; Woods, J.H.; and Stebbins, W.C. Effect of ethanol and of noise on reaction time in the monkey: Variation with stimulus level. Psychopharmacology 69:45-51, 1980.
Morrison, J.R., and Stewart, M.A. A family study of the hyperactive child syndrome. Biological Psychiatry 3:189-195, 1971.
Moskowitz, H., and Burns, M. Effects of alcohol and caffeine, alone and in combination, on skills performance. In: Goldberg, L., ed. Alcohol, Drugs and Traffic Safety. Vol. 3. Stockholm: Almqvist and Wiskell International, 1981. pp. 969-983.
Munjack, D.J., and Moss, H.B. Affective disorder and alcoholism in families of agoraphobics. Archives of General Psychiatry 38:869-871, 1981.
Myers, R.D., and Melchior, C.L. Alcohol drinking: Abnormal intake caused by tetrahydropapaveroline (THP) in the brain. Science 196:554-556, 1977.
Myers, R.D.; McCaleb, M.L.; and Ruwe, W.D. Alcohol drinking induced in the monkey by tetrahydropapaveroline (THP) infused into the cerebral ventricle. Pharmacology, Biochemistry and Behavior 16:995-1000, 1982.
National Highway Traffic Safety Administration. The Effects of Alcohol on the Driver's Visual Information Processing, by Ziedman, K.; Moskowitz, H.; and Niemann, R.A. DOT HS-805 748. Washington, D.C.: NHTSA, 1980. 131 pp. NTIS No. PB81-172751.
National Highway Traffic Safety Administration. Effects of Fatigue and Alcohol on Highway Safety, by Ryder, J.M.; Malin, S.A.; and Kinsley, C.H. DOT HS-805 854. Washington, D.C.: NHTSA, 1981. 114 pp. NTIS No. PB81-204117.
O'Leary, M.R.; Clasyn, D.A.; and Fauria, T. The group embedded figures test: A measure of cognitive style or cognitive impairment. Journal of Personality Assessment 44:532-537, 1980.
Orrego, H.; Blendis, L.M.; Blake, J.E.; Kapur, B.M.; and Israel, Y. Reliability of assessment of alcohol intake based on personal interviews in a liver clinic. Lancet 2:1354-1356, 1979.
Overall, J.E.; Brown, D.; Williams, J.D.; and Neill, L.T. Drug treatment of anxiety and depression in detoxified alcoholic patients. Archives of General Psychiatry 29:218-221, 1973.
Parker, E.S. Comments on "Cognitive functioning in men social drinkers. A replication study." Journal of Studies on Alcohol 43:170-177, 1982.
Parsons, O.A., and Fabian, M.S. Comments on "Cognitive functioning in men social drinkers. A replication study." Journal of Studies on Alcohol 43:178-182, 1982.
Parsons, O.A., and Leber, W.R. Alcohol, cognitive dysfunction, and brain damage. In: National Institute on Alcohol Abuse and Alcoholism. Biomedical Processes and Consequences of Alcohol Use. Alcohol and Health Monograph No. 2. DHHS Pub. No. (ADM)82-1191. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 213-253.
Pfefferbaum, A.; Horvath, T.B.; Roth, W.T.; Clifford, S.T.; and Kopell, B.S. Acute and chronic effects of ethanol on event-related potentials. In: Begleiter, H., ed. Biological Effects of Alcohol. Advances in Experimental Medicine and Biology. Vol. 126. New York: Plenum Press, 1980. pp. 625-639.
Pittman, Q.J.; Rogers, J.; and Bloom, F.E. Arginine vasopressin deficient Brattleboro rats fail to develop tolerance to the hypothermic effects of ethanol. Regulatory Peptides 4:33-41, 1982.
Pohorecky, L.A. Effects of ethanol on central and peripheral noradrenergic neurons. Journal of Pharmacology and Experimental Therapeutics 189:380-391, 1974.
Porjesz, B., and Begleiter, H. Evoked brain potential deficits in alcoholism and aging. Alcoholism: Clinical and Experimental Research 6(1):53-63, 1982.
Rabin, R.A.; Wolfe, B.B.; Dibner, M.D.; Zahniser, N.R.; Melchior, C.L.; and Molinoff, P.B. Effects of ethanol administration and withdrawal on neurotransmitter receptor systems in C57 mice. Journal of Pharmacology and Experimental Therapeutics 213:419-496, 1980.
Rangaraj, N., and Kalant, H. Interaction of ethanol and catecholamines on rat brain $(Na^+ + K^+)$-ATPase. Canadian Journal of Physiology and Pharmacology 57:1098-1166, 1979.
Rangaraj, N., and Kalant, H. Effect of chronic ethanol treatment on temperature dependence and on norepinephrine sensitization of rat brain $(Na^+ + K^+)$-adenosine triphosphatase. Journal of Pharmacology and Experimental Therapeutics 223:536-539, 1982.
Rhenstrom, S.; Simert, G.; Hansson, J.A.; Johnson, G.; and Vang, J. Chronic hepatic encephalopathy. A psychometrical study. Scandinavian Journal of Gastroenterology 12:305-311, 1977.
Ron, M.A.; Acker, W.; Shaw, G.K.; and Lishman, W.A. Computerized tomography of the brain in

chronic alcoholism. A survey and follow-up study. Brain 105:497-514, 1982.

Rosenthal, N.E.; Davenport, Y.; Cowdry, R.W.; Webster, M.H.; and Goodwin, F.K. Monoamine metabolites in cerebrospinal fluid of depressive subgroups. Psychiatry Research 2:113-119, 1980.

Rubin, L.S. Pupillometric studies of alcoholism. International Journal of Neurosciences 11:301-308, 1980.

Ryan, C. Learning and memory deficits in alcoholics. Journal of Studies on Alcohol 41:437-447, 1980.

Ryan, C. Alcoholism and premature aging: A neuropsychological perspective. Alcoholism: Clinical and Experimental Research 6:22-30, 1982.

Schenker, S.; Henderson, G.I.; Hoyumpa, A.M., Jr.; and McCandless, D.W. Hepatic and Wernicke's encephalopathies: Current concepts of pathogenesis. American Journal of Clinical Nutrition 33:2719-2726, 1980.

Schuckit, M.A. Prevalence of affective disorder in a sample of young men. American Journal of Psychiatry 139:1431-1436, 1982.

Shaw, S.; Gorkin, B.D.; and Lieber, C.S. Effects of chronic alcohol feeding on thiamin status: Biochemical and neurological correlates. American Journal of Clinical Nutrition 34:856-860, 1981.

Shefner, S.A.; Chiu, T.H.; and Anderson, E.G. Intracellular measurement of ethanol effects on rat locus caeruleus neurons in a brain slice preparation. Society for Neuroscience Abstracts 8:651(A.183.3), 1982.

Siggins, G.R., and Bloom, F.E. Alcohol-related electrophysiology. Pharmacology, Biochemistry and Behavior 13(Supplement 1):203-211, 1980.

Siggins, G.R.; Berger, T.; French, E.D.; Shier, T.; and Bloom, F.E. Ethanol, salsolinol and tetrahydropapaveroline alter the discharge of neurons in several brain regions: Comparison to opioid effects. In: Beta-Carbolines and Tetrahydroisoquinolines: Proceedings of a Workshop Held at the Salk Institute (1981). Progress in Clinical and Biological Research. Vol. 90. New York: Liss, 1982. pp. 275-285.

Sinclair, J.D.; Rusi, M.; Airaksinen, M.; and Altshuler, H.L. Relating TIQ's, opiates and ethanol. In: Bloom, F.; Barchas, J.; Sandler, M.; and Usdin, E., eds. Beta-Carbolines and Tetrahydroisoquinolines. Progress in Clinical and Biological Research. Vol. 90. New York: Liss, 1982. pp. 365-376.

Smith, H.H., and Smith, L.S. WAIS functioning of cirrhotic and non-cirrhotic alcoholics. Journal of Clinical Psychology 33:309-313, 1977.

Sorenson, S.; Dunwiddie, T.; McClearn, G.; Freedman, R.; and Hoffer, B. Ethanol-induced depression in cerebellar and hippocampal neurons in mice selectively bred for differences in ethanol sensitivity: An electrophysiological study. Pharmacology, Biochemistry and Behavior 14:227-234, 1981.

Sorenson, S.; Palmer, M.; Dunwiddie, T.; and Hoffer, B. Electrophysiological correlates of ethanol-induced sedation in differentially sensitive lines of mice. Science 210:1143-1145, 1980.

Stokes, J.A., and Harris, R.A. Alcohols and synaptosomal calcium transport. Molecular Pharmacology 22:99-104, 1982.

Tabakoff, B.; Luthin, G.L.; Saito, T.; and Hoffman, P.L. Effects of ethanol on receptor adenylate cyclase coupling (abstract). Federation Proceedings 42(4):902, 1983.

Tabakoff, B.; Munoz-Marcus, M.; and Fields, J.Z. Chronic ethanol feeding produces an increase in muscarinic cholinergic receptors in mouse brain. Life Sciences 25:2173-2180, 1979.

Tabakoff, B., and Hoffman, P.L. Development of functional dependence on ethanol in dopaminergic systems. Journal of Pharmacology and Experimental Therapeutics 208:216-222, 1979.

Tabakoff, B., and Ritzmann, R.F. The effects of 6-hydroxydopamine on tolerance to and dependence on ethanol. Journal of Pharmacology and Experimental Therapeutics 203:319-331, 1977.

Taberner, P.V. Sex differences in the effects of low doses of ethanol on human reaction time. Psychopharmacology 70:283-286, 1980.

Tarter, R.E.; McBride, H.; Buonpane, N.; and Schneider, D.U. Differentiation of alcoholics: Childhood history of minimal brain dysfunction, family history, and drinking pattern. Archives of General Psychiatry 34:761-768, 1977.

Ticku, M.K., and Burch, T. Alterations in gamma-aminobutyric acid receptor sensitivity following acute and chronic ethanol treatments. Journal of Neurochemistry 34:417-423, 1980.

Tong, J.E.; Henderson, P.R.; and Chipperfield, B.G.A. Effects of ethanol and tobacco on auditory vigilance performance. Addictive Behavior (Oxford) 5:153-158, 1980.

Tsuang, M.T. Genetic factors in suicide. Diseases of the Nervous System 38:498-501, 1977.

Tuomisto, L.; Airaksinen, M.M.; Peura, P.; and Erikson, C.J.P. Alcohol drinking in the rat: Increases following intracerebroventricular treatment with tetrahydro-Beta-carbolines. Pharmacology, Biochemistry and Behavior 17:831-836, 1982.

U.S. Department of Health and Human Services. Fourth Special Report to the U.S. Congress on Alcohol and Health. DeLuca, J.R., ed. DHHS Pub. No. (ADM)81-1080. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

U.S. Department of Health, Education, and Welfare. Second Special Report to the U.S. Congress on Alcohol and Health. Chafetz, M.E., ed. DHEW Pub. No. (ADM)75-212. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1974.

U.S. Department of Health, Education, and Welfare. Third Special Report to the U.S. Congress on Alcohol and Health. Noble, E.P., ed. DHEW Pub. No. (ADM)79-832. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1978.

Victor, M.; Adams, R.D.; and Collins, G.H. The Wernicke-Korsakoff Syndrome. Philadelphia: F.A. Davis, 1971.

Walker, D.W.; Hunter, B.E.; and Abraham, W.C. Neuroanatomical and functional deficits subsequent to chronic ethanol administration in animals. Alcoholism: Clinical and Experimental

Research 5:267-282, 1981.

Weingartner, H.; Cohen, R.M.; Murphy, D.L.; Martello, J.; and Gerdt, C. Cognitive processes in depression. Archives of General Psychiatry 38:42-47, 1981.

Weingartner, H.; Grafman, J.; Boutelle, W.; Kaye, W.; and Martin, P.R. Forms of memory failure. Science 221:372-373, 1980.

Weissman, M.M., and Myers, J.K. Clinical depression in alcoholism. American Journal of Psychiatry 137:372-373, 1980.

Wells, C.E. Diagnosis of dementia. Psychosomatics 20:517-522, 1979.

West, J.R.; Lind, M.D.; Demuth, R.M.; Parker, E.S.; Alkana, R.L.; Cassell, M.; and Black, A.C. Lesion-induced sprouting in the rat dentate gyrus is inhibited by repeated ethanol administration. Science 218:808-810, 1982.

Wilkinson, D.A. Examination of alcoholics by computed tomographic (CT) scans: A critical review. Alcoholism: Clinical and Experimental Research 6:31-45, 1982.

Wilkinson, D.A., and Carlen, P.L. Chronic organic brain syndromes associated with alcoholism: Neuropsychological and other aspects. In: Israel, Y.; Glaser. F.B.; Kalant, H.; Popham, R.E.; Schmidt, W.; and Smart, R.G., eds. Research Advances in Alcohol and Drug Problems. Vol. 6. New York: Plenum Press, 1981. pp. 107-145.

Wise, R.A. Actions of drugs of abuse on brain reward systems. Pharmacology, Biochemistry and Behavior 13(Suppl 1):213-223, 1980.

Wood, D.; Wender, P.H.; and Reimherr, F.W. The prevalence of attention deficit disorder, residual type, or minimal brain dysfunction, in a population of male alcoholic patients. American Journal of Psychiatry 140:95-98, 1983.

Wood, W.G., and Armbrecht, H.J. Behavioral effects of ethanol in animals: Age differences and age changes. Alcoholism: Clinical and Experimental Research 6:3-12, 1982.

Young, J.A., and Pihl, R.O. Self-control of the effects of alcohol intoxication. Journal of Studies on Alcohol 41:567-571, 1980.

Zornetzer, S.F.; Walker, D.W.; Hunter, B.E.; and Abraham, W.C. Neurophysiological changes produced by alcohol. In: National Institute on Alcohol Abuse and Alcoholism. Biomedical Processes and Consequences of Alcohol Use. Alcohol and Health Monograph No. 2. DHHS Pub. No. (ADM)82-1191. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 95-128.

Chapter IV

Medical Consequences of Alcohol

For most of us, alcohol conjures up pleasant social occasions--wine with a good meal, beer at a ball game, or cocktails during a party of friends. Rarely do we consider the harmful effects of alcohol. Even many experienced drinkers who know every vineyard, vintage year, distillery, and brewery are relatively unaware of the basic medical and biological consequences of drinking.

This chapter follows the trail of adverse effects of alcohol throughout the body and its impact on various organ systems.

Alcohol and the Digestive System

The Mouth

The application of dilute alcohol and a number of alcoholic beverages to the tongue and mucous membranes of the cheek stimulates the flow of saliva (Martin and Pangborn 1971). However, after a short time, the secretion rate of saliva is inhibited for 60 to 90 minutes before returning to normal (Winsor and Strongin 1933). Enlargement of the parotid (a specific salivary gland) is common in alcoholics (approximately 12 percent), but it is uncertain whether it occurs as a result of alcohol use or is due to the protein deficiency frequently seen in alcoholics (Bode 1981).

Inflammation of lips and soft tissue of the mouth, common in alcohol abusers, is thought to occur as a result of nutritional deficiency, particularly of the various B vitamins and iron (Larato 1972).

Cancers of the mouth, tongue, pharynx, and esophagus occur more often in alcoholics than in nonalcoholics. Wynder (1975) has suggested that a synergistic effect between alcohol and tobacco may be responsible. Other factors that may contribute to such carcinogenesis include deficiencies of vitamin A, vitamin B, and zinc that may occur in the alcoholic (Wynder and Chan 1970). Sporn et al. (1976) found that vitamin A deficient animals are more susceptible to cancers of the skin, mouth, and esophagus than are nondeficient animals.

The Esophagus

The occurrence of nonmalignant esophageal disease such as esophagitis has been associated with chronic alcohol abuse (Shirazi and Platz 1978). In normal human volunteers, alcohol has been shown to interfere with acid clearing mechanisms and to irritate the mucous membranes (Mayer et al. 1978). Mucosal tissue tends to be abnormal in alcoholics (Zeus 1970). Moreover, there is an increased risk of Barrett's esophagitis (a premalignant lesion) in alcoholics when compared with nonalcoholics (Martini and Wienbeck 1974). Esophageal varicose veins, which can develop in cirrhotic patients, can be eroded, resulting in bleeding into the gastrointestinal tract (Chaput et al. 1974).

The Stomach

The effect of alcohol on gastric emptying largely depends on the concentration of alcohol in the stomach (Cooke 1972). Gastric emptying is slowed when alcohol concentrations are greater than 6 percent (Pirola and Davis 1970).

While it has no effect on the muscle that empties the stomach, alcohol has been shown to produce a diminution in the sphincter muscle response to acidity in the duodenum (Phosawasdi et al. 1979).

Chronic consumption of alcohol causes a diminution of gastric acid secretion in humans (Cooke 1972). Furthermore, alcohol increases the formation of prostaglandins, which are known to inhibit acid secretion (Main and Whittle 1976). Such an increase may account for the reduced stomach acid observed in individuals who have abused alcohol for 5 or

more years. Acute administration of alcohol into the mouth, stomach, or blood, however, stimulates secretion of gastric juice. The secretion appears to be maximal at alcohol concentrations between 8 and 16 percent, approximately the concentration found in wine (Elwin 1969).

Acid often injures the mucous membranes of the stomach (Gottfried et al. 1976). Thus, drinking can produce gastric hemorrhage. While alcohol alone does not cause gastric bleeding in normal subjects, it significantly increases blood loss in persons with aspirin-derived mucous membranes injury (DeSchepper et al. 1978). Therefore, the aspirin commonly taken by alcohol abusers to alleviate discomfort may aggravate further stomach injury (Robert et al. 1980).

Alcohol abuse as a cause of gastric ulcer disease, however, remains controversial. Although the incidence of peptic ulcer has been reported to be as high as 20.6 percent in patients with alcoholic liver disease, an association between the two disease conditions has never been proven (Bode 1981).

There is conflicting evidence concerning the role of alcohol in stomach cancer, with most studies showing no clear association. However, a limited number of studies have shown a positive correlation between alcohol use and the development of gastric cancer (Bode 1981). Whether alcohol-induced gastritis is a premalignant lesion, particularly if it occurs repeatedly, is an important question for which sufficient evidence is not yet available (Bode 1981).

The Intestine

The intestine is an important site for the absorption of nutrients into the blood stream. The major focus of research in this area has been on the small intestine. This site is exposed to higher concentrations of alcohol than any other organ in the body except the stomach. After either acute or chronic alcohol consumption, the small intestine may demonstrate structural injury.

In humans, a single small dose (1 gm/kg body weight) of alcohol can produce lesions in the duodenum, a part of the small intestine (Gottfried et al. 1976). Additional studies with human volunteers found that the structural changes that occurred upon consumption of alcohol disappeared once alcohol consumption ceased (Rubin et al. 1972). Similarly, in rats, intestinal lesions occur within 10 minutes of alcohol ingestion, are well developed within an hour, and disappear after 4 to 16 hours (Baraona et al. 1974). This same study found that animals that chronically consumed alcohol did not respond with such lesions.

Decreases in intestinal enzymes, including those that act on milk, are common in experimental animals and man after alcohol ingestion. Thus, milk intolerance may be exaggerated in alcohol abusers (Perlow et al. 1975).

When applied directly to small intestinal membranes, alcohol decreases the sodium-potassium-ATPase activity from 94 percent to 17 percent of control values (Hoyumpa et al. 1977). As a result of this effect, alcohol in excess of 2 percent can inhibit the transport of electrolytes, amino acids, and glucose across the small intestine (Kuo and Shanbour 1978). Thus, both in animals and in humans, alcohol inhibits the transport of essential amino acids (Israel et al. 1968). Although tissue damage resulting from large amounts of alcohol can inhibit amino acid transport, the fact that it is rapidly reversible suggests that a physiochemical change rather than a toxic injury is responsible (Israel et al. 1968).

Vitamin absorption is adversely affected by alcohol. Alcoholics have shown a significant reduction in the absorption of folic acid (a vitamin) into the jejunum, another part of the small bowel (Halsted et al. 1973). However, after 2 weeks of nutritional supplementation, the folic acid absorption of alcoholics improves despite continued use of alcohol. This suggests that, in alcoholics, impaired folic acid absorption may be primarily a result of poor nutrition rather than a direct toxic effect of alcohol. In support of this contention, studies of acute alcohol administration to normal subjects have shown a decreased folic acid absorption in only 20 percent of the subjects studied (Halsted et al. 1967). However, folic acid deficiency is the most common nutritional deficiency present in alcoholics (Leevy et al. 1965). There also is evidence to suggest that liver tissue is less able to take up folic acid from blood after acute alcohol administration to either normal or alcoholic individuals (Lane et al. 1976).

Thiamine (vitamin B_1) is absorbed much like folic acid. The active absorption of thiamine by cells lining the small intestine is not affected by alcohol (Hoyumpa et al. 1974). However, thiamine movement out of the intestinal cell is impaired by alcohol (Hoyumpa et al. 1975). Both human and animal studies suggest that alcohol inhibits the mechanism

for absorption of thiamine at normal levels of the vitamin (Thomson et al. 1970), but has no effect on the diffusion mechanism that comes into play at high thiamine concentrations (Hoyumpa et al. 1974).

Alcohol's effect on iron absorption is unclear. In one human study (Charlton et al. 1964), a single dose of alcohol increased absorption of a dietary form of iron, ferrous chloride, while others have found no effect of either acute or chronic alcohol administration on iron absorption (Murray and Stein 1965). Adding further confusion to this issue are the studies that showed that ferrous iron absorption is inhibited rather than enhanced by alcohol (Tapper et al. 1968).

Although high levels of zinc are commonly found in the urine of alcoholics, it has not been established that alcohol consumption produces zinc deficiency by increased urinary zinc losses (Sullivan 1962). While alcohol is metabolized by a zinc-containing enzyme, zinc deficiency is not known to decrease alcohol metabolism (Wang and Pierson 1975).

The mechanism involved in calcium transport by the small intestine has not been elucidated. An animal study showed that alcohol inhibits calcium absorption (Krawitt 1975), but the mechanism of such inhibition is not entirely clear. In contrast to animal studies, one study of nonalcoholics given short-term alcohol showed no adverse effect on calcium absorption (Verdy and Caron 1973). Others, however, have reported a doubling of fecal calcium in human volunteers after drinking, suggesting a reduced calcium absorption (Krawitt 1975).

Alcohol has multiple effects on lipid metabolism within the small intestine. In general, alcohol increases triglyceride synthesis in intestines and in mucous membranes (Baraona et al. 1975). It also causes a decrease in fatty acid oxidation.

After exposure to alcohol, the intestinal lymph glands produce more cholesterol and triglyceride, an effect seen only when alcohol is present within the intestine (Middleton et al. 1971). In addition, cholesterol is redistributed among the various intestinal lymph lipoproteins. If alcohol is injected rather than drunk, the redistribution does not occur. This suggests that alcohol acts on the small intestine mucosal enzymes in altering the synthesis and transport of cholesterol. Interestingly, chronic alcohol feeding to animals abolishes or inhibits these acute effects of alcohol on intestinal lipid transport (Baraona et al. 1975; Rodgers and O'Brien 1975). Thus, the relationship of these findings to the clinical condition of alcohol-induced hyperlipidemia (excess lipids in the blood) remains unclear (Baraona et al. 1975).

The effect of alcohol on the motility of different small intestine segments is variable, but the net effect is to shorten the transit time through the intestine. Initially, when intravenous alcohol is given to volunteers, motility increases, particularly in the second portion of the duodenum (Pirola and Davis 1970). This increased motility is characterized by an increase in intestinal pressure and in the number of contractile waves generated. Later, there is a decrease in duodenal activity with a gradual return toward normal. Moreover, alcohol depresses nonpropulsive motility of the colon in both dogs and humans. It should be noted that these changes in small and large intestinal motor activity may contribute, at least in part, to the diarrhea commonly seen following excessive drinking (Martin et al. 1980).

The Pancreas

Excessive alcohol use can cause chronic pancreatitis, in which lesions and functional impairment persist even in the absence of alcohol (Sarles 1974). This contrasts with gallstone-induced acute pancreatitis in which the pancreas returns to normal after each episode.

More than 75 percent of the cases of chronic pancreatitis in the United States occur in alcoholics. Moreover, pathologic changes or alterations in pancreatic function can be detected in half the alcoholics without pancreatitis symptoms (Reber 1978). Steady alcohol consumption over about 6 to 12 years is necessary before pancreatic symptoms occur.

Acute pancreatitis usually does not occur in the nonalcoholic who occasionally drinks excessively (Strum and Spiro 1971). On the other hand, alcoholics develop symptoms of acute pancreatitis, but only after functional and histologic (tissue) changes of chronic pancreatitis are well established. Progressive destruction of the pancreas continues even after the individual stops drinking.

Surprisingly, chronic alcohol administration to dogs stimulates pancreatic secretion, whereas alcohol's acute effect is inhibitory (Brooks and Thomas 1953). This excitatory effect can be abolished by atropine (a drug that blocks some nervous system activities) and does not occur in previously vagotomized (cutting the nerves connecting the brain to the stomach) dogs. Again, the neurochemical

mechanism acting on alcoholic animals is opposite to that seen in nonalcoholic animals. The reason why chronic alcoholism reverses this acute effect of alcohol on the pancreas is not known.

Regardless of the specific mechanism involved, chronic alcohol consumption results in the secretion of a juice more concentrated in protein. Protein precipitates are rich in calcium carbonate and are identical to the small pancreatic stones found in humans with chronic pancreatitis (Nakamura et al. 1972). In both dogs and humans, these "plugs" of precipitated protein obstruct the ducts, blocking secretion. Acetaldehyde is a highly labile and reactive substance that readily forms adducts with proteins. If sufficient amounts of acetaldehyde are present in the pancreas, it may contribute to the formation of pancreatic stones which obstruct the ducts.

The fine structural changes that occur in the pancreas after alcohol ingestion are similar to those found in liver cells (Darle et al. 1970), and the changes in early human chronic pancreatitis appear to be similar to those observed in animals chronically treated with the hormones gastrin or cholecystokinin.

A relatively recent finding is that a specific genetically controlled cell surface antigen (a substance that activates the immune system) has an increased prevalence in individuals with chronic pancreatitis due to alcoholism. This suggests a possible genetic mechanism predisposing alcoholics to pancreatitis (Fauchet et al. 1979).

An association between alcoholism and cancer of the pancreas has been hypothesized. Burch and Ansari (1968) were the first to make such a suggestion, based on a retrospective study in which 75 percent of the patients with pancreatic cancer also had a history of moderate to heavy alcohol intake. Additional support for this thesis was provided by the report that the risk of pancreatic cancer was twice as great in males who consumed alcohol daily as it was in nondrinkers (Lieber 1977).

Alcohol and the Liver

Until recently, it was unclear whether liver disease associated with alcohol consumption was a direct effect of the alcohol or of the malnutrition that often accompanies alcoholism. The landmark work, primarily of Lieber (1981) and his colleagues, has now established that alcohol is directly toxic to the liver.

Metabolism of Alcohol

Alcohol is not effectively stored in tissues, and little less than 10 percent of an ingested dose can be eliminated through the kidneys, lungs, and skin. For practical purposes, one can assume that the body rids itself of alcohol only by oxidizing it in the liver, the organ containing the bulk of the enzymes required for alcohol oxidation. The liver's complexity and unique role in alcohol oxidation contribute to the many deleterious effects of alcohol within the liver. Unlike other major sources of calories, alcohol cannot be stored either in the liver or in other tissues; it must therefore be metabolized immediately in preference to all other fuels.

Three liver enzyme systems have been shown to promote the oxidation of alcohol to acetaldehyde. They are, in descending order of importance: alcohol dehydrogenase (ADH), microsomal ethanol-oxidizing system (MEOS), and catalase. The acetaldehyde produced is itself toxic, so a second step is subsequently required to convert it to a final nontoxic substance, acetate.

The major pathway for alcohol metabolism involves ADH. Although an increase in ADH activity above that seen normally may not necessarily increase the rate of alcohol oxidation, reductions in ADH activity do diminish alcohol metabolism (Bosron and Li 1980). Thus, low protein diets, which reduce ADH levels, slow the metabolism of alcohol both in rats and in humans (Pekkanen et al. 1978). Consistent with this observation, prolonged fasting reduces the metabolism of alcohol (Bode and Thiele 1975). Moreover, the sex steroid testosterone inhibits ADH activity while estradiol, an estrogen, enhances it (Rachamin et al. 1980).

As noted above, other systems in addition to ADH can oxidize alcohol. Thus, in animal experiments, as much as 30 percent of the total chronically administered alcohol may be oxidized by a non-ADH enzyme pathway in which MEOS plays the major role (Matsuzaki et al. 1981). However, the contribution of this system to alcohol elimination in humans has not been quantitated. The issue in humans is complicated by the presence of many forms of ADH, including one form, the π ADH, which has an activity profile similar to MEOS (Bosron et al. 1979). Nonetheless, following chronic alcohol consumption, the MEOS system is significantly increased in activity (Lieber and DeCarli 1968).

In humans, alcohol consumption accelerates blood alcohol clearance, particularly at high alcohol concentrations. This observation is consistent with the metabolic activity of MEOS (Salaspuro and Lieber 1978) but is also consistent with the activity of ▼ ADH. MEOS activity generates only heat, while ADH oxidation can produce storable forms of energy. This may account for the observation that alcohol produces a greater increase in oxygen consumption in alcoholics than in normal individuals, and also for the lesser growth in animals that are fed alcohol as compared to their controls (Pirola and Lieber 1972). Such energy wasting could explain, at least in part, the weight loss experienced when alcohol calories are substituted for a balanced diet (Lieber et al. 1965).

Alcohol oxidation always produces acetaldehyde which, in turn, is metabolized to acetate. It is generally accepted that more than 90 percent of the acetaldehyde formed as a consequence of alcohol oxidation is oxidized by aldehyde dehydrogenase (ALDH) to acetate immediately within the liver.

The principal cellular site of acetaldehyde metabolism lies within the mitochondria, which are found in the cytoplasm of cells. Moreover, the major portion of acetaldehyde oxidation within the mitochondria occurs where ALDH is located.

Acetaldehyde, like its precursor alcohol, adversely affects many tissues. It appears to interfere with vitamin B_6 metabolism and promotes the vitamin's degradation (Veitch et al. 1975). Acetaldehyde has been shown to impair the synthesis of proteins in the heart and can inhibit protein secretion by liver cells (Schreiber et al. 1972, 1974; Sorrell et al. 1983). Finally, acetaldehyde can depress the capacity of the liver to oxidize fatty acids (Cederbaum et al. 1975). The alcoholic may therefore be a victim of a vicious cycle; high acetaldehyde levels and chronic alcohol consumption impair the liver's mitochondrial function, which decreases acetaldehyde metabolism, which accelerates the accumulation of acetaldehyde, all leading to liver damage.

Amino Acid and Protein Metabolism

Alcohol disrupts amino acid (the building blocks of proteins) metabolism in the liver, which leads to their excessive accumulation (Krebs et al. 1973). Amino acid abnormalities in the blood appear in patients with alcoholic hepatitis, cirrhosis, and liver insufficiency (Rosen et al. 1977). In an isolated rat liver, relatively high concentrations of alcohol inhibit the uptake of amino acids (Krebs et al. 1973).

Patients with cirrhosis frequently have an increased plasma level of aromatic amino acids (Ono et al. 1978). These amino acids convert to amines within the gastrointestinal tract and can adversely affect the central nervous system by acting as false neurotransmitters. In this regard, Faraj and coworkers (1976,1979) found a statistically significant correlation between the level of plasma tyramine (an amino acid product) and the degree of hepatic encephalopathy (liver-caused brain damage).

The level of alpha amino N-butyric acid (AANB) in the blood is increased after chronic alcohol consumption, which has led to suggestions that it may be of use as a biochemical marker or indicator of alcoholism (Shaw et al. 1976). However, the plasma level of AANB may reflect at least two different factors present in chronic alcoholic individuals: Chronic alcohol consumption tends to increase the level of AANB, while dietary protein deficiency tends to decrease it. It is therefore necessary to control for nutritional factors if one is to use the level of AANB in plasma as a biochemical marker of chronic alcohol consumption (Shaw and Lieber 1978).

Alcoholics with cirrhosis and malnutrition have depressed hepatic levels of carnitine, an amino acid needed for oxidation of fatty acids (Rudman et al. 1977). Possibly this is due to an impaired ability of such patients to synthesize it. The blood level of free proline (an amino acid) is higher in some patients with cirrhosis compared with controls (Rojkind and DeLeon 1970) and appears to be proportional to the collagen (the structural protein that accumulates in cirrhosis) content of the livers of such individuals (Kershenobich et al. 1970).

Increased levels of acetaldehyde have been noted in patients with alcohol-induced liver disease, and acetaldehyde, but not alcohol, has been shown to interfere with protein synthesis (Schreiber et al. 1972, 1974; Sorrell et al. 1983). Consistent with this finding is the observation that alcohol does not inhibit protein synthesis by those liver cells that do not oxidize alcohol to form acetaldehyde (Morland et al. 1979). A similar lack of an inhibitory effect occurs in a variety of nonhepatic tissues in which the ADH activity is absent or less than that present in the liver (Perin and Sessa 1975). Thus, the inhibitory effects of alcohol on protein synthesis are dependent, at least in part, on alcohol metabolism to acetaldehyde.

Fatty Acid Metabolism

Fatty infiltration of the liver after alcohol consumption is the most common hepatic abnormality associated with alcohol abuse. The infiltration is due to an increased accumulation of triglycerides in response to alcohol. The origin of the triglycerides depends upon the pattern of alcohol consumption (dose and duration) and the lipid content of the diet. With acute ingestion of a large dose of alcohol, the excess hepatic triglycerides are derived from peripheral fat stores, while after chronic alcohol ingestion, the excess of triglycerides is the result of fat synthesis by the liver itself.

The replacement of dietary triglycerides containing long chain fatty acids with fat consisting of medium chain triglycerides reduces the propensity of alcohol to induce a fatty liver (Lieber and DeCarli 1966). Apparently the greater propensity of medium chain triglycerides to undergo oxidation accounts for this phenomenon (Lieber 1967). Protein deficiency may also contribute to an alcohol-induced fatty liver in some circumstances; however, even with adequate protein in the diet, alcohol may cause the development of fatty liver. It would appear that the main factors leading to the development of alcoholic fatty liver are as follows: Alcohol replaces fatty acids as the preferred fuel for mitochondria. The metabolic consequence is that more lipid (fatty acid) is synthesized and less is burned. In addition, alcohol at high concentrations inhibits the transport of newly synthesized lipids out of the liver cell. The net effect is accumulation of fatty acids.

A consequence of the hepatic accumulation of fatty acid is the excess formation of ketones (Lefevre et al. 1970). This results in alcoholic ketoacidosis (increased levels of ketones and acids in the blood), which is usually associated with a mild hyperglycemia (elevated blood sugar). Susceptibility to alcoholic ketoacidosis varies among individuals. The basis for alcoholic ketoacidosis is still unclear; however, its development may not be related to the amount of alcohol ingested nor to the levels of alcohol in the blood. It is possible that disrupted hormone levels are involved. Blood insulin levels are low during the ketoacidosis episode, while those of growth hormone, epinephrine, glucagon, and cortisol are high. Such a hormone pattern could act to mobilize free fatty acids from peripheral adipose (fat) tissue to enhance fatty acid metabolism by the liver and contribute to the mild hyperglycemia.

Other Metabolic Effects

Chronic alcohol ingestion leads to proliferation of liver microsomes, fine intracellular structures that are responsible for detoxifying many drugs. Therefore, it is not surprising that an enhanced metabolism of drugs is common in alcoholics. For example, the metabolism of meprobamate, pentobarbital, antipyrine, tolbutamide, warfarin, and diphenylhydantoin is enhanced after heavy alcohol intake and can persist for up to 3 weeks after alcohol intake has been discontinued (Mezey 1979).

Chronic drinking is associated with a raised metabolic rate, which is characterized by increased oxygen consumption, inefficient use of calories, increased heat output, and weight loss (Pirola and Lieber 1972). This hypermetabolic state has been hypothesized to result, at least in part, from increased enzyme activity within the liver (Israel et al. 1973). The increased rate of oxygen consumption can be markedly depressed by surgically removing the thyroid and can be abolished by treatment with propylthiouracil (PTU), a thyroid inhibitor (Orrego et al. 1979). These observations suggest that PTU may be of potential therapeutic value in alcoholic patients with liver disease. Indeed, in a recent study, PTU was reported to exert a beneficial short-term effect on both the magnitude and the rate of improvement in patients with alcoholic hepatitis (Orrego et al. 1979). Moreover, the therapeutic value of PTU was found to be greatest in those patients with the most severe liver disease. There are, however, some conflicting reports. For example, Halle et al. (1982) performed a double-blind controlled trial in patients with severe acute alcoholic hepatitis. No beneficial effects of PTU therapy were observed. The question of the therapeutic usefulness of PTU therefore remains to be answered.

Pathology

There are three specific subtypes of hepatic pathology associated with alcohol use: alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. In its early stages, alcoholic liver disease is characterized by accumulation of excess fat in the liver as a result of the mechanisms already described above. Alcoholic hepatitis is characterized by the death and inflammation of individual liver cells. This

more severe form of alcohol-associated hepatic injury may cause death in 10 to 30 percent of the afflicted individuals. Eventually the entire structural and functional capacity of the liver is impaired, resulting in cirrhosis, the most severe and presumably irreversible form of alcohol-induced liver disease.

Most patients with alcoholic fatty liver are virtually asymptomatic; the various laboratory tests appear nearly normal. Importantly, alcoholic fatty liver is a completely reversible lesion that does not necessarily progress to a more severe disease.

The study of patients with alcoholic hepatitis may lead to an understanding of the natural evolution of alcoholic liver disease culminating as cirrhosis. In some populations, particularly in Europe and Japan, cirrhosis develops in alcoholics without an apparent intermediate stage of alcoholic hepatitis (Karasawa et al. 1980). This observation raises the question as to whether alcohol can promote the development of cirrhosis without being preceded by a stage of alcoholic hepatitis. It now appears from both human and animal studies that alcoholic hepatitis may not be necessary for the development of alcoholic cirrhosis (Popper and Lieber 1980).

According to a new theory, the balloon-like swelling characteristic of alcoholic hepatitis develops as a result of the accumulation within the cell of lipid and protein, which normally would have been secreted into the blood. The retention of such proteins presumably results from degenerative effects of alcohol on subcellular structures (microtubules) that are important for the secretory activity of the liver (Matsuda et al. 1979). Thus, the effect of alcohol may be similar to that of drugs which bind to the cellular proteins and produce lesions similar to those seen in human liver cells with prolonged alcohol use (Derr et al. 1979).

The severity of the various alcohol-associated pathologies of the liver correlates poorly with either the duration of drinking or the amount of alcohol consumed.

Not all patients with alcoholic hepatitis develop cirrhosis, and alcoholic hepatitis appears to occur in 29 percent of male and 47 percent of female alcoholics (Wilkinson et al. 1969; Morgan and Sherlock 1977; Gavaler 1982). Since specific histocompatibility antigens (HLA) are more prevalent in patients with cirrhosis than in controls, these genetic factors might determine an alcoholic's susceptibility to develop cirrhosis (Goodwin 1971; Bell and Nordhagen 1980).

Alcohol and Muscle Systems

Heart Muscle

An association between alcoholism and heart disease has been recognized for more than 100 years. Until recently, however, heart disease was thought to result from malnutrition, particularly thiamine deficiency, and not alcohol itself. Now that thiamine deficiency has been eliminated as an important contributing factor, heart disease has been directly linked to alcoholism.

Specifically, cardiomyopathy, a primary disorder of heart muscle, is often found in chronic heavy drinkers. It generally appears in patients with a long history of alcohol consumption, usually somewhat greater than 10 years in duration. The major symptoms of alcohol cardiomyopathy are chronic shortness of breath and signs of congestive failure such as edema, chest pain, fatigue, palpitations, and blood-stained sputum.

Alcoholic cardiomyopathy does not occur suddenly (Demakis et al. 1974). It gradually progresses from a subclinical condition characterized by minimal cardiac findings and nonspecific electrocardiographic abnormalities to overt congestive heart failure. The severity of the illness appears to be related directly to the duration of alcohol abuse. The prospect for recovery is reasonably good, if the individual ceases to drink, but recovery is slow and may require 5 to 6 years (Fuster et al. 1981).

It is generally believed that damage to the cell mitochondria of the heart muscle is the major mechanism responsible for alcoholic cardiomyopathy (Alexander 1967). Electron microscopic studies clearly show degenerative changes of the mitochondria in response to chronic drinking (Alexander 1967; Alexander et al. 1977b). Other subcellular structures also may be abnormal, leading to depression of mitochondrial respiration, liberation of mitochondrial enzymes, and a reduction of energy-providing ATP in the heart (Alexander et al. 1977a).

In contrast, some epidemiological studies have indicated that alcohol in moderate doses may have a health enhancing effect on the risk for coronary heart disease (Klatsky 1980). However, it has also been shown that at mildly intoxicating doses alcohol adversely affects left ventricular function (Ahmed et al. 1973). Larger doses actually impair the ability of the heart muscle to contract. Thus, alcohol depresses the heart muscle function at blood

concentrations found during alcohol intoxication. Gimeno and coworkers (1962) observed such depression in rats at concentrations of alcohol as low as 0.1 percent. Spann and his colleagues (1968) found that heart contractions of left ventricular muscles, obtained from both normal cats and those with chronic heart failure, are slowed by alcohol. As the alcohol dose is increased, the heart muscle contractions continue to be slowed. Nakano and Moore (1972) observed a similar heart muscle velocity/alcohol dose relationship in guinea pigs.

Delgado and his associates (1975) observed that consuming one to two drinks of Scotch whisky affected the heart in normal subjects 30 to 90 minutes following ingestion. Similarly, Ahmed et al. (1973) found that whisky ingested over 2 hours by normal subjects resulted in a reduction of the duration of systole.

The peripheral circulatory and neurohormonal effects of alcohol tend to obscure the unfavorable action of alcohol on the heart. Both acetaldehyde and acetate (metabolites of alcohol) have been shown to have direct effects on the vascular system resulting in vasodilatation (dilated blood vessels) (Liang and Lowenstein 1978). Acetate also increases cardiac output and left ventricular peak pumping rate and reduces the resistance of peripheral blood vessels, all varying with the alcohol dose (Liang and Lowenstein 1978).

Interestingly, alcohol cannot be metabolized by the heart because alcohol dehydrogenase is absent in the heart (Lochner et al. 1969). Acetaldehyde dehydrogenase is present, however, and thus acetaldehyde can be and is metabolized by cardiac muscle (Forsyth et al. 1973). Despite this lack of alcohol metabolism, Regan and his associates (1969) have shown that following alcohol administration to dogs various ions and enzymes usually found only inside cells are released by heart muscle into the blood. This leakage of cellular contents presumably indicates cellular damage, suggesting that alcohol itself is toxic to the heart. Moreover, Swartz and coworkers (1974) have reported that calcium uptake and binding in the heart, which is needed for muscle contraction, is inhibited by alcohol. Furthermore, Williams and his coworkers (1975) have demonstrated a dose-dependent inhibition of the sodium-potassium-ATPase activity of blood vessel membranes isolated from guinea pig hearts, with both alcohol and acetaldehyde. The enzyme plays a critical role in controlling the amounts of sodium and potassium, necessary for muscle contraction, in the cell.

Cardiac arrhythmias (heart beat irregularities), such as ventricular fibrillation and palpitations, are common in individuals with alcohol-related disease and, in particular, during alcohol intoxication (Ettinger et al. 1978; Greenspon et al. 1981). Gould and his coworkers (1969) have suggested that sudden death probably caused by cardiac arrhythmias may be relatively common among young adults who are found, at autopsy, to have large fatty livers, presumably due to alcohol abuse. It is likely that these alcohol-induced cardiac arrhythmias are due to the direct effects of alcohol upon the heart muscle as well as to the adverse effects of acetaldehyde upon the conduction system. As little as 2 ounces of whisky, consumed by individuals with existing organic heart disease, can suppress the heart's ability to generate muscle contractions that pump the blood throughout the body (Newman and Valicenti 1971). Moreover, another study has indicated that alcohol intoxication can result in a complete heart block (absence of heart beat), requiring pacemaker therapy (Leier et al. 1974).

Finally, it appears that patients with existing heart disease are sensitive to adverse myocardial effects of alcohol or acetaldehyde (Conway 1968; Gould et al. 1971).

Skeletal Muscle

Myopathy, the disease of skeletal muscle, has been associated with alcohol abuse for about 120 years. Modern concepts of alcoholic myopathy began, however, in 1955 with the studies of Ekbom and his associates (1964), who first described a syndrome of muscle weakness without evidence of other signs or symptoms in alcoholics. Eventually, a wide spectrum of alcoholic myopathy has come to be recognized, from the completely asymptomatic to the near fatal (Hed et al. 1962).

Subclinical myopathies occur in more than one-third of alcoholics. Some alcoholics will have a history of muscle cramps, weakness, and occasional episodes of dark urine (myoglobinurea) which is thought to be due to the presence of myoglobin released by damaged muscle tissue (Faris et al. 1967).

The development of muscle weakness in any alcohol-abusing individual could imply acute alcoholic myopathy. Such individuals may experience a sudden attack of muscle pain or a rapid progression of a previously diagnosed chronic myopathy. Such attacks can be fatal. Generally, the muscles are exquisitely tender

during attacks, and are centered in one group of muscles, although on occasion the effect can be diffuse. Fortunately, if alcohol use is discontinued, the disease and its symptoms disappear.

Smooth Muscle

Alcohol's effects on smooth muscle have been recognized only recently. Previously, when alcohol was used as an analgesic for pregnant women, the uterine muscles occasionally stopped contracting. This led researchers to speculate that alcohol directly inhibited smooth muscle contractions (Chapman and Williams 1951). This concept was challenged, however, when Fuchs and Wagner (1963) reported that alcohol interfered with the release of oxytocin, a hormone responsible for uterine contractions, and that this inhibition of hormone activity was the major factor responsible for the diminished uterine contractions. However, more recently, several research teams have shown that alcohol in low concentrations does indeed directly depress uterine contractions (Gimeno et al. 1971; Laversen et al. 1973).

Moreover, Fischer et al. (1965), Winship and his associates (1968), Hogan et al. (1972), and Kjellen and Tibbling (1978) have reported that alcohol reduces sphincter (a smooth muscle) pressure in the lower esophagus. Even more recently, Altura and colleagues (1976, 1978) have shown that both alcohol and acetaldehyde consistently enlarge the peripheral blood vessels, by relaxation of the smooth muscle in the vessel walls.

Alcohol and Blood Disorders

Prolonged protein deprivation and deficiency of B vitamins, particularly riboflavin, pyridoxine, and folic acid, play a role in reducing the formation of new blood cells. In animal studies, protein deficiency or the removal of even a single essential amino acid from the diet can produce anemia with reduced blood formation in the bone marrow, which recovers after resuming a normal diet (Chitis et al. 1963). Thus, protein deprivation probably plays an important role in the production of both the anemia and the abnormal iron levels seen in alcoholics, particularly those with liver disease.

The close relationship of folic acid deficiency to chronic alcoholism has been recognized for years. Consumption of a folate-poor diet for several months will deplete body stores, and the diet of most alcoholics contains significantly less than the daily minimum requirement of this vitamin (Wu et al. 1975). Therefore, folic acid deficiency is the primary cause of megaloblastic (abnormal red blood cells) anemia in alcoholics (Sullivan and Herbert 1964; Hines and Cowan 1974). Because folic acid deficiency causes ineffective production of red blood cells, it is associated with increased iron turnover in the blood and a delayed red blood cell incorporation of iron. Therefore, folic acid deficiency leads to increased iron absorption and may be responsible for the increased iron stores in some chronic alcoholics. Impaired liver function may also contribute to these effects. Not only is folate intake reduced, but in individuals with alcoholic liver disease, folate may be released from stores in the liver and lost in the urine, therefore further reducing folate stores (Cherrick et al. 1965). Thus, folate deficient alcoholics may need to be treated with folic acid in therapeutic doses much larger than the amount needed to simply maintain normal function.

The symptoms of riboflavin deficiency, which include anemia, underdeveloped bone marrow, and abnormalities in developing blood cells, are identical to those seen in chronic drinkers. Thus, riboflavin deficiency may also contribute to the anemia present in alcoholics.

Vitamin B_6 is ineffectively converted to its active coenzyme form in alcoholics (Lumeng and Li 1974). The coenzyme deficiency appears to cause several clinical problems in alcoholics, including some forms of anemia as well as changes in the bone marrow, peripheral neurological disease, convulsions, and worsening of liver disease (Davis and Smith 1974; Hines 1975).

Finally, it is possible that alcohol itself may inhibit heme (a constituent of hemoglobin) synthesis in red blood cells (Moore 1974; Ibrahim et al. 1979).

Most alcoholics without iron deficiency have enlarged red blood cells (macrocytosis), a recognized but poorly understood disorder (Binghman 1960). Such blood cell dysmorphology may be the result of a variety of underlying mechanisms, including (1) folate deficiency, (2) increased numbers of immature red blood cells, and (3) increased deposition of cholesterol and phospholipids in red cell membranes, associated with liver disease.

Unger and Johnson (1974) were the first to report that, during routine screening of employees of an insurance company, a number of

alcoholics were discovered to have an elevated MCV (mean corpuscular volume, or average blood cell size) in the absence of other changes usually associated with alcoholism, such as folate deficiency, increased numbers of immature red blood cells, or significant liver disorder. Since then, many reports have confirmed their observations (Buffet et al. 1975; Morin and Porte 1976; Davidson and Hamilton 1978; Wright and Ree 1978). An increased MCV has been found in about 90 percent of alcoholics, which suggests that the MCV may be useful as a marker for alcoholism (Unger and Johnson 1974; Buffet et al. 1975; Morin and Porte 1976). Furthermore, in several large population studies, the number of alcoholic drinks taken daily correlated with the MCV (Whitehead et al. 1978; Eschwege et al. 1978). Even with abstention, little or no change in the MCV occurs for many weeks; usually 2 to 4 months of abstention are required before the MCV returns to normal (Unger and Johnson 1974).

Leukopenia (a reduced number of white blood cells) is relatively common in alcoholics (Cowan and Hines 1971). Eichner et al. (1972), for example, observed leukopenia in 8 percent of their cases. Other studies found 1.6 percent (Eichner 1973) and 8.5 percent (Liu 1973) of subjects with leukopenia.

Bone marrow smears obtained from such individuals consistently show a decreased number of cells with markedly decreased numbers of mature granulocytes. The leukopenic episodes in alcoholics tend to be transient, lasting 2 to 4 days, and usually followed by rapid recovery and an increased number of white blood cells.

As long ago as 1938, Pickrell noted in rabbits that white blood cells (which kill intruding bacteria) were inhibited from moving into sites of bacterial infections within the skin and lung during alcohol intoxication. He noted also that the white blood cells attacked the bacteria normally. Similar results have been obtained in mice (Louria 1963) and in humans (Brayton et al. 1970). MacGregor and his associates (1974; Gluckman et al. 1977) have shown that alcohol inhibits the movement of human white blood cells. Alcohol consumption for as short as 6 to 8 days can result in such inhibition. The mechanism by which alcohol impairs such white blood cell functions remains unclear, although it has been suggested that increased intracellular concentrations of cyclic AMP (adenosine monophosphate) after consuming alcohol may be partly responsible for this phenomenon.

There is additional evidence of altered immunologic activity of white blood cells in alcoholics. Studies of animals and humans during periods of alcohol ingestion found that the immunologic response of the skin was reduced (Gluckman et al. 1977). Also, many patients with alcoholic hepatitis have an altered immunity to liver antigens (Young et al. 1979). Furthermore, lymphocytes (one type of white blood cell) from patients with alcoholic liver disease may attack the patients' own liver cells (Paronetto and Lieber 1976). In summary, these observations suggest that abnormalities of lymphocytic function occur in alcoholics and that immunologic mechanisms may account for some of the liver damage induced by alcohol even after abstinence (Lue et al. 1979).

The natural tendency for the blood to coagulate and seal a bleeding wound is disrupted in alcoholics, principally as a complication of advanced liver disease. These changes are similar to those occurring in patients with other chronic liver diseases. Most often, the levels of the clotting factors dependent on vitamin K are decreased. Moreover, the clotting compounds themselves may be abnormal in alcoholics (Weinstein and Deykin 1978; Conoso et al. 1979).

Alcohol and Kidney Disease

Alcoholics with liver disease may have enlarged kidneys with increased fat, protein, and water (Van Thiel et al. 1977). Seven to 14 percent of alcoholics, about 20 times the rate of nonalcoholics, suffer tissue loss in their kidneys (Edmondson et al. 1966; Longacre and Popky 1968). In one study, 12 of 20 alcoholics suffered kidney tissue loss during their first attack of acute kidney infection, with the lower urinary tract the source in most cases. These infections occurred in alcoholics without cirrhosis, suggesting that alcohol abuse and not liver disease was the cause. Such a conclusion is warranted because kidney infection does not accompany other types of severe liver disease.

Alcohol and Pulmonary Disease

Chronic obstructive pulmonary disease is common among alcohol-abusing males, especially smokers (Rankin et al. 1969). Other pulmonary problems such as pneumococcal pneumonia are more likely to occur in alcoholics than in the general population. It is

possible that poor dental health, combined with recurrent abnormal respiration (aspiration) during intoxication, may be responsible for the increased prevalence of bacterial lung abscesses in alcoholics. Tuberculosis is a well-recognized health problem in malnourished alcoholics, and impaired connections between the arteries and veins in the lungs of alcoholics, especially those with advanced liver disease, can cause cyanosis (reduced hemoglobin), hyperventilation, and hypoxia.

Alcohol and the Endocrine System

Gonadal and Adrenal Effects

Low levels of androgens (male hormones) are found in alcoholic men. Thus, 70 to 80 percent experience decreased libido and/or impotence (Van Thiel 1980). In addition, 70 to 80 percent of such men show both testicular atrophy and infertility (Van Thiel and Lester 1979a).

Not only do alcoholic men produce fewer androgens, but such men also produce excess estrogens, the female hormones. Fifty percent of alcoholic men with cirrhosis develop feminine pubic hair patterns, and 20 percent develop enlarged mammary glands (Van Thiel and Lester 1979a). These signs of chronic alcoholism, unlike the transient impotence commonly experienced with an acute alcoholic bout, persist even in the absence of intoxication and are due in large measure to alcohol-induced tissue injury.

Until recently, liver disease was considered to be a primary cause of the sexual dysfunction present in alcoholics. During the past 10 years, however, this concept has been severely challenged, and a diametrically opposite view has gained currency (Van Thiel and Lester 1979a). This recent view is the result of evidence showing that sexual dysfunction can be present in alcoholic men with essentially normal livers (Van Thiel et al. 1974b). Plasma levels of testosterone, a male hormone, are reduced in men within hours after drinking enough alcohol (approximately seven drinks) to produce a hangover (Ylikahri et al. 1974). Many of the features of alcohol-induced sexual dysfunction can be produced in experimental animals with normal livers (Van Thiel et al. 1975a, 1979a). Furthermore, alcohol reduces testosterone levels in mice and rats (Van Thiel and Lester 1979a). Thus, the concept that the sexual changes observed in alcoholic men are the result of alcohol per se, rather than the indirect consequences of alcohol-induced liver disease, has gained considerable credence.

The specific mechanisms by which alcohol adversely affects testicular function are being unraveled slowly. Vitamin A is essential for creating sperm, and alcohol may interfere with vitamin A activation in the testes (Van Thiel et al. 1974a). Alcohol metabolism may shift the balance between essential enzymes in the testes as it does in the liver, thereby limiting the generation of testosterone (Van Thiel and Lester 1976a). Similarly, acetaldehyde, either produced in the testes or entering the testes from the blood as a result of alcohol metabolism outside the testes, may have deleterious effects upon testicular mitochondria, subcellular organelles that are critical for generating steroids (Gavaler et al. 1983). Indeed, the conversion of cholesterol to the steroid pregnenolone, a reaction that occurs in mitochondria, is inhibited when mitochondria are exposed either to alcohol or to acetaldehyde. Several studies have found a reduced capacity to produce steroids in the testes obtained from alcohol-fed rats (Chiao et al. 1981; Cicero et al. 1980).

Not only is testicular testosterone production inhibited as a result of alcohol exposure, but recent studies have demonstrated that alcohol interferes with gonadotropin (a substance that stimulates the gonads) binding to testicular tissue. Furthermore, chronic drinking is associated with a pituitary-endocrine defect for gonadotropin secretion (Van Thiel et al. 1978c). Alcoholics thus have low gonadotropin concentrations in their blood and respond inadequately to stimuli such as luteinizing hormone releasing factor that provoke gonadotropin release (Van Thiel et al. 1978c). Similar inadequate gonadotropin responses can be demonstrated in chronic alcohol-fed rats and after acute alcohol administration to normal rats (Van Thiel et al. 1979a). The cumulative evidence suggests that chronic drinking induces gonadal injury through its direct effects on the gonad, as well as through indirect effects on the hypothalamus (a part of the brain that integrates endocrine activity) and the pituitary gland.

In addition to having reduced gonad performance, alcoholic men also have relatively high levels of estrogens (Van Thiel and Lester 1976b, 1979a). As noted earlier, they show many of the secondary sex characteristics of women. Such femininization results from increases in estrogen-responsive proteins and the hormone neurophysin (Van Thiel et al. 1975b). The increases in the hormone prolactin

(associated with milk production) seen in cirrhosis are also probably related to estrogen (Van Thiel et al. 1978d). Because atrophy of the testes can be produced by estrogen, the testicular damage observed in alcoholic men with cirrhosis can also be ascribed to excess estrogens. Blood levels of one estrogen, estradiol, are either normal or slightly increased in alcoholic men, and indeed, some estrogen levels, e.g., estrone, are increased moderately (Van Thiel et al. 1974b, 1975b; Van Thiel and Lester 1976a, 1979a). This finding of normal or increased estrogen levels in the presence of androgen deficiency is paradoxical, since estrogens can be produced only by conversion from preformed androgens. The presence of normal or moderately increased blood estrogen levels thus requires further explanation.

Preliminary results suggest that increased estrogens are the result of both the direct effects of alcohol and indirect effects mediated through the development of liver disease. Contrary to initial expectations, however, the metabolic clearance rate for estradiol in men with alcoholic cirrhosis has been found to be normal, not reduced. Evidence is accumulating to suggest that adrenal overproduction of weak estrogen precursors regularly occurs in alcoholic men (Southren et al. 1973; Olivo et al. 1975; Gordon et al. 1975; Van Thiel et al. 1980). Furthermore, signs of excess adrenal steroids resembling Cushing's syndrome have been described in such men. These patients develop loss of peripheral muscle mass, obesity, hypertension, facial redness, increased cortical steroid levels in the blood, and loss of the normal diurnal variation of the steroid cortisol in the blood. The mechanism responsible for this overproduction of estrogen-precursors is unknown.

In contrast to the male, the alcoholic female is not superfeminized but instead shows severe gonadal failure commonly manifested by reduced or absent menstruation, loss of secondary sex characteristics such as breast and pelvic fat accumulation, and infertility. Studies of ovaries from alcoholic women who died of cirrhosis while still in their reproductive years (20 to 40 years of age) have shown a paucity of developing ovarian follicles and few or no corpora lutea, both of which are necessary for successful pregnancy (Jung and Russfield 1972). Moreover, these findings have been reproduced recently in animals (Van Thiel et al. 1978a).

The failure of the ovaries to produce hormones in alcoholic women is manifested by reduced blood levels of estradiol and progesterone, loss of secondary sex characteristics, and inability to ovulate. The biochemical mechanisms for such failure are probably the same as those occurring within the testes of the male, as the pathways for generating steroids are the same in the gonads of the two sexes. An alcohol dehydrogenase, seen in the ovaries of alcoholic women, may contribute to endocrine failure.

In addition to a direct effect on the gonads, chronic alcoholics, whether male or female, also showed evidence of a defect in the control by the brain over sex hormone secretion (Gordon et al. 1979). Thus, despite severe gonadal injury, follicle-stimulating hormone levels in the female, expected to increase to correct gonad failure, are well below levels expected for the degree of reproductive failure present.

The Hypothalamic-Pituitary-Adrenal Axis

The hypothalamus, deep inside the brain, is the master hormone controller. It sends hormones to the pituitary gland, which in turn emits other hormones to other glands, including the adrenal gland. This system is called the hypothalamus-pituitary-adrenal axis. Early studies on animals showed that alcohol changes the activity of the adrenal cortex (Hion-Jon 1925; Smith 1951; Forbes and Duncan 1951; Czaja and Kalant 1961; Ellis 1966). These changes could be prevented by removing the pituitary gland. A sharp decrease in the pituitary hormone ACTH (adrenocorticotropin hormone) (Noble et al. 1971) caused by alcohol suggested that the primary effect of alcohol is at the pituitary level rather than at the adrenal gland itself (Ellis 1966).

In normal humans, intoxicating doses of alcohol produce an immediate increase in the blood level of the steroid cortisol (Fazekas 1966). The cortisol response appears to parallel the blood alcohol level. This acute response in normal individuals is probably due to a hypothalamic stress reaction and pituitary release of ACTH.

In contrast to this acute stress reaction, animal studies found that alcohol intoxication and withdrawal are associated with inhibition of the release of corticotropin releasing factor (CRF) and impairment of the ACTH stress response (Tabakoff et al. 1978).

Researchers have recently begun to study the effect of endogenous (naturally occurring within the nervous system) opiates (enkepha-

lins and endorphins) on the control of pituitary releasing factors. Such opiates appear to inhibit CRF and thereby ACTH release. They therefore might contribute to reduced ACTH release seen during alcohol intoxication and withdrawal (Morley et al. 1980). This hypothesis is consistent with other observations that opiates alter some of alcohol's effects. For example, the opiate antagonist, naloxone, improves the psychomotor impairment and depressed level of consciousness induced by alcohol (Jeffcoate et al. 1979; Jefferys et al. 1980).

The urine of patients with cirrhosis, especially those with edema, contains increased amounts of the steroid aldosterone, which controls the amount of fluid and salt in the body (Bongiovanni and Eisenmenger 1951). Individuals with cirrhosis are likely to have an increased secretion rate and blood levels of aldosterone (Coppage et al. 1962).

Chronic liver disease is associated with a significantly decreased blood flow in the liver, the site where aldosterone is metabolized. As a result, the clearance of aldosterone from the body is reduced and the duration of the activity of the hormone is prolonged (Coppage et al. 1962). It should be noted, however, that the resultant elevated blood levels of aldosterone in cirrhotic individuals reflect not only a decreased metabolic clearance but also an increased secretion rate of the hormone occurring, at least in part, in response to an increased production of angiotensin, which stimulates aldosterone secretion.

The state of the hypothalamic-pituitary-adrenal axis during alcohol withdrawal has been studied extensively in animals. After alcohol is withdrawn from mice, they are likely to be hyperactive, with seizures and increased corticosteroids in the blood (Goldstein 1972). Chronic alcoholics also experience increased corticosteroid levels during alcohol withdrawal (Stokes 1973).

Interestingly, the pituitary reserve of ACTH in alcoholics experiencing withdrawal is frequently reduced (Wright et al. 1975). Alcoholics who abstain from drinking often show persistent abnormalities of the hypothalamic-pituitary-adrenal axis (Oxenkrug 1978).

In addition to altering steroid hormone release by the adrenal gland, alcohol stimulates the secretion of catecholamines, e.g., epinephrine and norepinephrine, and increases the adrenal content of catecholamine synthesizing enzymes (Pohorecky 1974). Studies in rats have suggested that acetaldehyde is principally responsible for these observed changes in catecholamine secretion in response to alcohol (Walsh and Truitt 1970).

The Thyroid

The most consistent effect of alcohol on the function of the thyroid is to moderately decrease the hormone thyroxine (T_4) levels in the blood and to markedly decrease the hormone triiodothyronine (T_3) in the blood (Israel et al. 1979). It has been suggested that the low T_3 levels after alcohol consumption reflect injury to the liver and reduced ability of the liver to remove iodine from T_4 (Orrego et al. 1979). Despite the considerable data suggesting that alcohol affects the thyroid (and its interactions with the hypothalamus and pituitary) indirectly via the liver, alcohol can directly cause an increase in the thyroid uptake of iodine, which is needed to synthesize the thyroid's hormones (Yadav et al. 1970). Moreover, Wright (1978) and Van Thiel et al. (1979b) have reported a diminished thyroid stimulating hormone (TSH) response to thyrotropin releasing factor (TRH) in alcoholics.

Growth Hormone and Prolactin

Considerable evidence suggests that alcohol blocks the release of growth hormone. Early studies of laboratory animals suggested that alcohol produces degenerative changes in the pituitary (Sanchez-Calvo 1941). More recently, the acute administration of large doses of alcohol to rats has been shown to abolish spontaneous growth hormone secretion (Redmond 1980). Alcoholics with cirrhosis, in contrast, have elevated levels of growth hormone and frequently respond abnormally to stimuli of growth hormone (Van Thiel et al. 1978b).

Two studies (Torro et al. 1973; Earll et al. 1976) have reported that a single dose of alcohol had no effect on prolactin (a hormone associated with milk-stimulation as well as other functions). However, Loosen and Prange (1977) reported reduced prolactin levels, but with minimally impaired prolactin responses to TRH during alcohol withdrawal. Jung and Russfield (1972) reported an increased prevalence of prolactin-secreting cells in the pituitaries of male and female patients who died of alcoholic liver disease. Ylikahri et al. (1976) noted increased prolactin responses to TRH in alcoholics, a finding confirmed by Van Thiel and his coworkers (1978a, b, c, d). Van Thiel and his associates (1978a, b, c, d) also reported that elevated prolactin levels occur in cir-

rhosis, and that cirrhotics have reduced prolactin responses to TRH. In contrast, individuals with fatty liver have reduced prolactin levels and exaggerated prolactin responses to TRH. Preliminary studies in the rat also suggest that alcohol increases prolactin levels in the blood (Gordon and Southren 1977).

Vasopressin and Oxytocin

Alcohol produces diuresis, which seems to occur because the hormone vasopressin, the body's antidiuretic hormone, is inhibited. Indeed, several groups have found reduced vasopressin levels after acute alcohol administration (Linkola et al. 1977; Helderman et al. 1978). Little or no tolerance to the diuretic effects of alcohol or its inhibition of vasopressin release has been observed in alcoholics (Marquis et al. 1975). Alcohol's suppression of vasopressin release appears to originate in the hypothalamus. Thus, stimuli applied directly to the hypothalamus can override the diuretic effects of alcohol. Alcohol may, however, inhibit the electrically evoked discharges of the hypothalamus (Raiha 1960).

More recently, studies showed that vasopressin was suppressed while blood alcohol levels were increasing. After the maximum blood alcohol levels were attained, the vasopressin levels increased (Marquis et al. 1975).

On the basis of bioassay data, alcohol would appear to inhibit the release of the hormone oxytocin, which is the principal uterine-contracting and lactation-stimulating hormone of the pituitary gland (Wagner and Fuchs 1968). No data, however, are available on the actual blood levels of oxytocin during alcohol administration and withdrawal.

Parathormone

Alcohol causes hypocalcemia (reduced blood calcium) in both dogs and rats (Peng et al. 1972). Parathormone, the parathyroid hormone that controls blood calcium levels, does not reverse this hypocalcemic effect of alcohol (Peng and Gitelman 1974). The fall in calcium may be related to the shift of calcium ions out of the blood (Peng et al. 1972). Some studies in normal volunteers and in alcoholics have suggested that alcohol produces an increased urinary excretion of both calcium and magnesium (Kalbfleisch et al. 1963; Jones et al. 1969). Alcohol has been shown to reduce the transport of calcium in the duodenum (Krawitt 1975). The defect in calcium stability found in alcoholics with hypocalcemia, however, is most likely due to an alcohol-induced decrease in blood magnesium levels (Estep et al. 1969). Magnesium is well known to be important in the regulation of parathormone secretion and in the mediation of the hormone's peripheral action (Rasmussen 1974). Both malabsorption of calcium and a primary dietary deficiency of vitamin D probably are responsible, at least in part, for the hypocalcemia in individuals with advanced alcoholic cirrhosis. Finally, Williams and his coworkers (1978) recently have reported that alcohol results in an increased level of the hormone calcitonin, which may play a role in developing hypocalcemia.

It is of some interest that a decreased density of tibial bone has been reported in rats chronically fed alcohol (Saville and Lieber 1965). Alcoholic patients do have a decreased bone mass and an increased incidence of fractures (Nilsson 1970). Finally, low phosphate in the blood, which also is common in alcoholics, may contribute to the development of the metabolic bone disease seen in alcoholics (Knochel 1977).

The Endocrine Pancreas

Several studies have shown that alcohol increases insulin secretion in response to glucose (Singh and Patel 1976; Shah et al. 1977). Interestingly, alcohol increases the insulin response to other compounds that stimulate secretion as well as to glucose (Kuhl and Anderson 1974).

Glucose intolerance is common in individuals with alcoholic liver disease, particularly those with portal hypertension (Phillips and Safrit 1971; Kreisberg et al. 1972). Insulin and especially glucagon (a hormone that ultimately increases blood glucose) levels are increased in such individuals (Marco et al. 1973). It is thought that the glucose intolerance in such individuals is due primarily to raised levels of glucagon in the blood. However, abnormal glucose tolerance can occur in alcoholics due to chronic pancreatitis as well as to advanced liver disease.

The syndrome of fasting alcoholic hypoglycemia (low blood sugar) develops within 6 to 36 hours after ingestion of alcohol by a previously malnourished or fasting individual. No age group appears to be exempt from this type of alcohol-induced reaction, but children and women seem to be particularly susceptible. Several studies have reported that alcohol is capable of producing severe and conceivably fatal hypoglycemia in susceptible subjects (Marks and Medd 1964; Arky and Frienkel

1966). In addition to children, athletes are at particular risk for the development of severe hypoglycemia following the combination of alcohol ingestion, fasting, or exercise (Arky et al. 1968).

Alcohol and Cancer

Evidence for the strong associations between chronic alcohol consumption and cancers of the mouth, pharynx, larynx, and esophagus has existed for many years (Lieber et al. 1979). In addition to the cancers of the upper respiratory and alimentary tracts, more recent studies indicate that alcohol may play a role in cancers of the liver, pancreas, stomach, large intestine, rectum, breast, and malignant melanoma (Williams and Horm 1977; Rosenberg et al. 1982; Tuyns 1978).

There are no supporting data from animal studies to clearly show that alcohol by itself is carcinogenic. This issue is further clouded by the fact that, either by accident or as a result of the production process, carcinogenic materials were formerly found in various alcoholic beverages. These substances include nitrosamines, polycyclic hydrocarbons, fusel oils, and asbestos fibers (McGlashan et al. 1968; Wehman and Plantholt 1974; Spiegelholder et al. 1979).

While the basis for the relationship between alcohol and cancer is unknown, it is estimated that alcohol by itself, or in combination with substances such as tobacco, is associated with 3 percent of the cancer deaths in the United States (Rothman 1980; Doll and Peto 1981).

The interaction between alcohol consumption and tobacco is particularly striking in terms of cancers of the mouth, pharynx, and larynx, where the total risk is increased in a synergistic manner (Rothman and Keller 1972; Tuyns 1978; McCoy and Wynder 1979; Schottenfeld 1979). As an example, one study indicated that alcohol consumption and heavy smoking produced up to a fifteenfold increase in the risk of oral cancer, compared with the chances of people who neither drank nor smoked. Heavy smoking alone increased the risk by only twofold to threefold (Lemon et al. 1964; Lyon et al. 1976; Phillips 1980).

Despite the absence of a known mechanism of action, it is clear that heavy alcohol consumption is a risk factor for the development of cancer. To account for this action, several hypotheses have been generated, including: alcohol acting as a solvent to increase the entry of carcinogens into cells (McCoy and Wynder 1979); alcohol-induced enzyme changes leading to the conversion of procarcinogens (noncarcinogenic substances) into active carcinogens (Seitz et al. 1981a,b; Garro et al. 1981); and repeated alcohol-induced cellular damage promoting cancer in the liver (Lieber 1969).

Summary

Chronic alcohol consumption leads to ubiquitous toxic effects in the body, with medical consequences ranging from slight functional impairment to life-threatening disease states. The most common site of injury is the liver, the organ most responsible for ridding the body of alcohol.

In the early stages of alcoholic liver disease, the liver becomes fatty, a condition that may progress to hepatitis. After an extended period of chronic drinking, the liver structure may be affected, followed by a breakdown in its functional capacity. The result is cirrhosis--an often fatal disease.

Because the liver is so essential for metabolism and detoxification, many organs and body systems may be adversely affected indirectly by alcoholic liver disease. Excessive alcohol also may directly injure the gastrointestinal tract, muscles, and pancreas. As alcohol and its metabolites travel through the body in the blood stream, they may affect the major body systems, including the cardiovascular system, the nervous system, and the endocrine system. Furthermore, there is evidence of a strong association between chronic alcohol use and cancer of the stomach, large intestine, pancreas, and liver.

Many of alcohol's deleterious consequences are the result of effects on the endocrine system hormones. For example, fewer androgens are produced in alcoholic men, often leading to a femininization of their appearance, decreased libido, and infertility. Alcoholic women are affected also, frequently with ovarian dysfunction. Alone, and in conjunction with dietary deficiencies frequently associated with alcoholism, alcohol abuse can produce nutrition-related deficits in the body. These deficits result in altered protein metabolism and vitamin-related disorders such as anemia.

References

Ahmed, S.S.; Levinson, G.E.; and Regan, T.J. Depression of myocardial contractility with low doses of ethanol in normal man. Circulation 48: 378-385, 1973.

Alexander, C.S. Electron microscopic observations in alcoholic heart disease. British Heart Journal 29:200-206, 1967.

Alexander, C.S.; Forsyth, G.W.; and Nagasawa, H.T. Alcoholic cardiomyopathy in mice: Myocardial glycogen, lipids and certain enzymes. Journal of Molecular and Cellular Cardiology 9:235-245, 1977a.

Alexander, C.S.; Sekhri, K.K.; and Nagasawa, H.T. Alcoholic cardiomyopathy in mice: Electron microscopic observations. Journal of Molecular and Cellular Cardiology 9:247-254, 1977b.

Altura, B.M.; Carella, A.,; and Altura, B.T. Acetaldehyde on vascular smooth muscle: Possible role in vasodilator action of ethanol. European Journal of Pharmacology 52:73-83, 1978.

Altura, B.M.; Edgarian, H.; and Altura, B.T. Differential effects of ethanol and mannitol on contraction of anterial smooth muscle. Journal of Pharmacology and Experimental Therapeutics 197(2):352-361, 1976.

Arky, R.A., and Frienkel, N. Alcohol hypoglycemia. V. Alcohol infusion to test gluconeogenesis in starvation, with special reference to obesity. New England Journal of Medicine 274:426-433, 1966.

Arky, R.A.; Veverbrants, E.; and Abramson, E.A. Irreversible hypoglycemia; a complication of alcohol and insulin. Journal of the American Medical Association 206:575-578, 1968.

Baraona, E.; Pirola, R.C.; and Lieber, C.S. Small intestine damage and changes in cell population produced by ethanol ingestion in the rat. Gastroenterology 66:226-234, 1974.

Baraona, E.; Pirola, R.C.; and Lieber, C.S. Acute and chronic effects of ethanol on intestinal lipid metabolism. Biochimica et Biophysica Acta 388: 19-28, 1975.

Bell, H., and Nordhagen, R. HLA antigens in alcoholics with special reference to alcoholic cirrhosis. Scandinavian Journal of Gastroenterology 15:453-456, 1980.

Binghman, J. The macrocytosis of hepatic disease. II. Thick macrocytes. Blood 15(2):244-254, 1960.

Bode, J.C.H. Alcohol and the gastrointestinal tract. In: Bode, J.C.H., ed. Systemic Illness and the Gastrointestinal Tract. Stuttgart: Georg Thieme, 1981.

Bode, J.C., and Thiele, D. Hemmung des Aethanolabbaus beim Menschen durch Fasten: Reversibilitaet durch Fructose-Infusion [Inhibition of ethanol catabolism in humans through fasting: Reversibility through fructose infusion]. Deutsche Medizinische Wochenschrift 100:1849-1851, 1975.

Bongiovanni, A,M., and Eisenmenger, W.J. Adrenal cortical metabolism in chronic liver disease. Journal of Clinical Endocrinology and Metabolism 11:152-172, 1951.

Bosron, W.F., and Li, T.-K. Alcohol dehydrogenase. In: Jakoby, W.B., ed. Enzymatic Basis of Detoxification. Vol. 1. New York: Academic Press, 1980. pp. 231-248.

Bosron, W.F.; Li, T.-K.; Dafeldecker, W.P.; and Vallee, B.L. Human liver pi-alcohol dehydrogenase: Kinetic and molecular properties. Biochemistry 18:1101-1105, 1979.

Brayton, R.G.; Stokes, P.E.; Schwartz, M.S.; and Louria, D.B. Effect of alcohol and various diseases on leukocyte mobilization, phagocytosis and intracellular bacterial killing. New England Journal of Medicine 282:123-128, 1970.

Brooks, F.P., and Thomas, J.E. The effect of alcohol on canine external pancreatic secretion. Gastroenterology 23:36-42, 1953.

Buffet, C.; Choput, J.-C.; and Albuisson, F. La macrocytose dans l'hepatite alcoolique chronique histologiquement prouvee [Histologically confirmed macrocytosis in chronic alcoholic hepatitis]. Archives Francaises des Maladies de l'Appareil Digestif 64:309-315, 1975.

Burch, G.E., and Ansari, A. Chronic alcoholism and carcinoma of the pancreas: A correlative hypoth- esis. Archives of Internal Medicine 122:273- 275, 1968.

Cederbaum, A.I.; Lieber, C.S.; and Rubin, E. Effect of acetaldehyde on fatty acid oxidation and ketogenesis by hepatic mitochondria. Archives of Biochemistry and Biophysics 169:29-41, 1975.

Chapman, E.R., and Williams, P.T. Intravenous alcohol on an obstetrical analgesia. American Journal of Obstetrics and Gynecology 61:676-679, 1951.

Chaput, J.-C.; Petite, J.-P.; Gueroult, N.; Buffet, C.; Regensberg, M.; and Etienne, J.-P. La fibroscopie d'urgence dans les hemorrhagies digestives des cirrhoses: A propos de 100 cas [Emergency fibroscopy in digestive hemorrhages in cirrhosis: 100 cases]. Nouvelle Presse Medicale 3:1227-1230, 1974.

Charlton, R.W.; Jacobs, P.; Stefel, H.; and Bothwell, J.H. Effect of alcohol on iron absorption. British Medical Journal 2:1427-1429, 1964.

Cherrick, G.R.; Baker, H.; Frank, O.; and Leevy, C.M. Observations on hepatic avidity for folate in Laennec's cirrhosis. Journal of Laboratory and Clinical Medicine 66:446-451, 1965.

Chiao, Y.-B.; Johnston, D.E.; Gavaler, J.S.; and Van Thiel, D.H. Effect of chronic ethanol feeding on testicular content of enzymes required for testosteronogenesis. Alcoholism: Clinical and Experimental Research 5:230-236, 1981.

Cicero, T.J.; Bell, R.D.; Meyer, E.R.; and Badger, T.M. Ethanol and acetaldehyde directly inhibit testicular steroidogenesis. Journal of Pharmacology and Experimental Therapeutics 213:228-233, 1980.

Cohen, B.I., and Raicht, R.F. Effect of ethanol on

sterol metabolism in the rat (abstract). Alcoholism: Clinical and Experimental Research 4:212, 1980.

Conoso, R.T.; Hutton, R.A.; and Deykin, D. The hemostatic defect of chronic liver disease. Kinetic studies using ^{75}Se-selenomethionine. Gastroenterology 76:540-547, 1979.

Conway, N. Hemodynamic effects of ethyl alcohol in coronary heart disease. American Heart Journal 76:581-582, 1968.

Cooke, A.R. Ethanol and gastric function. Gastroenterology 62:501-502, 1972.

Coppage, W.S.; Island, D.P.; Cooner, A.E.; and Liddle, G.W. The metabolism of aldosterone in normal subjects and in patients with hepatic cirrhosis. Journal of Clinical Investigation 41: 1672-1680, 1962.

Cowan, D.H., and Baunach, D.C. Platelet cyclic AMP reduction in alcohol-related thrombocytopathia. Abstracts of the Meeting of the American Society of Hematology, p. 198, 1976.

Cowan, D.H., and Hines, J.D. Thrombocytopenia of severe alcoholism. Annals of Internal Medicine 74:37-43, 1971.

Czaja, C., and Kalant, H. The effect of acute alcohol intoxication on adrenal ascorbic acid and cholesterol in the rat. Canadian Journal of Biochemistry 39:327-334, 1961.

Darle, N.; Ekholm, R.; and Edlund, Y. Ultrastructure of the rat exocrine pancreas after long term intake of ethanol. Gastroenterology 58:62-72, 1970.

Davidson, R.J.L., and Hamilton, P.J. High mean red cell volume: Its incidence and significance in routine haematology. Journal of Clinical Pathology 31:493-498, 1978.

Davis, R.E., and Smith, B.K. Pyridoxal and folate deficiency in alcoholics. Medical Journal of Australia 2:357-360, 1974.

Delgado, C.E.; Fortuin, N.J.; and Ross, R.S. Acute effects of low doses of alcohol on left ventricular function by echocardiography. Circulation 51:535-540, 1975.

Demakis, J.G.; Proskey, A.; Rahimtoola, S.H.; Jamil, M.; Sutton, G.C.; Rosen, K.M.; Gunnar, R.M.; and Tobin, J.R. The natural course of alcoholic cardiomyopathy. Annals of Internal Medicine 80:293-297, 1974.

Denk, H.; Franke, W.W.; Eckerstorfer, R.; Schmid, E.; and Kerjaschki, D. Formation and involution of Mallory bodies ("alcoholic hyalin") in murine and human liver revealed by immunofluorescence microscopy with antibodies to prekeratin. Proceedings of the National Academy of Sciences of the United States of America 76:4112-4116, 1979.

DeSchepper, P.J.; Tjandramaga, T.B.; DeRoo, M.; Verhaest, L.; Daurio, C.; Steelman, S.L.; and Tempero, K.F. Gastrointestinal blood loss after diflunisal and after aspirin: Effect of ethanol. Clinical Pharmacology and Therapeutics 23:669-676, 1978.

Doll, R., and Peto, R. The causes of cancer: Quantitative estimates of avoidable risks of cancer in the United States today. Journal of the National Cancer Institute 66:1191-1308, 1981.

Earll, J.M.; Gaunt, K.; Earll, L.A.; and Djuh, Y.Y. Effect of ethyl alcohol on ionic calcium and prolactin in man. Aviation, Space, and Environmental Medicine 47:808-810, 1976.

Edmondson, H.A.; Reynolds, T.B.; and Jacobson, H.G. Renal papillary necrosis with special reference to chronic alcoholism: A report of 20 cases. Archives of Internal Medicine 118:225-264, 1966.

Eichner, E.R. The hematologic disorders of alcoholism. American Journal of Medicine 54:621-630, 1973.

Eichner, E.R.; Buchanan, B.; Smith, J.W.; and Hillman, R.S. Variations in the hematologic and medical status of alcoholics. American Journal of the Medical Sciences 263:35-42, 1972.

Ekbom, K.; Hed, R.; Kirstein, L.; and Astrom, K.-E. Muscular affections in chronic alcoholism. Archives of Neurology 10:449-458, 1964.

Ellis, F.W. Effect of ethanol on plasma corticosterone levels. Journal of Pharmacology 153: 121-127, 1966.

Elwin, C.-E. Some factors influencing the stimulatory effect of ethanol on gastric acid secretion during antrum application. Acta Physiologica Scandinavica 75:12-27, 1969.

Eschwege, E.; Papor, L.; Lellouch, J.; and Claude, J.R. Blood cells and alcohol consumption with special reference to smoking habits. Journal of Clinical Pathology 31:654-658, 1978.

Estep, H.; Shaw, W.A.; Watlington, C.; Hobe, R.; Holland, W.; and Tucker, S.-G. Hypocalcemia due to hypomagnesemia and reversible parathyroid hormone unresponsiveness. Journal of Clinical Endocrinology 29:842-848, 1969.

Ettinger, P.O.; Wu, C.F.; De la Cruz, C.; Weisse, A.B.; Ahmed, S.S.; and Regan, T.J. Arrythmias and the "holiday heart": Alcohol-associated cardiac rhythm disorders. American Heart Journal 95:555-562, 1978.

Faraj, B.A.; Bowen, P.A.; Isaacs, J.W.; and Rudman, D. Hypertyraminemia in cirrhotic patients. New England Journal of Medicine 294:1360-1364, 1976.

Faraj, B.A.; Fulenwider, J.T.; Rypins, E.B.; Nordlinger, B.; Ivey, G.L.; Jansen, R.D.; Ali, F.M.; Camp, V.M.; Kutner, M.; Schmidt, F.; and Rudman, D. Tyramine kinetics and metabolism in cirrhosis. Journal of Clinical Investigation 64: 413-420, 1979.

Faris, A.A.; Reyes, M.G.; and Abrams, B.M. Subclinical alcoholic myopathy; Electromyographic and biopsy study. Transactions of the American Neurological Association 92:102-106, 1967.

Fauchet, R.; Genetet, B.; Gosselin, J.; and Gastrad, J. HLA antigens in chronic alcoholic pancreatitis. Tissue Antigens 13:163-166, 1979.

Fazekas, I.G. Hydrocortisone content of human blood, and alcohol content of blood and urine, after wine consumption. Quarterly Journal of Studies on Alcohol 27:439-446, 1966.

Fischer, R.A.; Ellison, G.W.; Thayer, W.R.; Spiro, H.M.; and Glaser, G.H. Esophageal motility in neuromuscular disorders. Annals of Internal Medicine 63:229-248, 1965.

Forbes, J.C., and Duncan, G.M. The effect of acute alcohol intoxication on the adrenal glands of rats and guinea pigs. Quarterly Journal of Studies on Alcohol 12:355-359, 1951.

Forsyth, G.W.; Nagasawa, H.T.; and Alexander, C.S. Acetaldehyde metabolism by the rat heart. Proceedings of the Society for Experimental Biology and Medicine 144:498-500, 1973.

Fuchs, A.-R., and Wagner, G. The effect of ethyl alcohol on the release of oxytocin in rabbits. Acta Endocrinologica 44:593-605, 1963.

Fuster, V.; Gersh, B.J.; Giuliani, E.R.; Tajik, A.J.; Brandenburg, R.O.; and Frye, R.L. The natural history of idiopathic dilated cardiomyopathy. American Journal of Cardiology 47:525-531, 1981.

Garro, A.J.; Seitz, H.K.; and Lieber, C.S. Enhancement of dimethylnitrosamine metabolism and activation to a mutagen following chronic ethanol consumption. Cancer Research 41:120-124, 1981.

Gavaler, J.S. Sex-related differences in ethanol-induced liver disease: Artifactual or real? Alcoholism: Clinical and Experimental Research 6:186-196, 1982.

Gavaler, J.S.; Perez, H.A.; Estes, L.; and Van Thiel, D.H. Morphologic alterations of rat Leydig cells induced by ethanol. Pharmacology, Biochemistry and Behavior 18(Supplement 1):341-347, 1983.

Ghitis, J.; Piazuelo, E.; and Vitale, J.J. Cali-Harvard nutrition project. III. The erythroid atrophy of severe protein deficiency in monkeys. American Journal of Clinical Nutrition 12:452-454, 1963.

Gimeno, A.L.; Gimeno, M.F.; and Webb, J.L. Effects of ethanol on cellular membrane potentials and contractility of isolated rat atrium. American Journal of Physiology 203:194-196, 1962.

Gimeno, M.F.; Bedners, A.S.; DeVastik, F.J.; and Gimeno, A.L. Effect of ethanol on the motility of isolated rat myometrium. Archives Internationales de Pharmacodynamie et de Therapie 191:213-219, 1971.

Gluckman, S.J.; Dvorak, V.C.; and MacGregor, R.R. Host defenses during prolonged alcohol consumption in a controlled environment. Archives of Internal Medicine 137:1539-1543, 1977.

Goldstein, D.B. An animal model for testing effects of drugs on alcohol withdrawal reactions. Journal of Pharmacology and Experimental Therapeutics 183:14-22, 1972.

Goodwin, D.W. Is alcoholism hereditary? A review and critique. Archives of General Psychiatry 25:545-549, 1971.

Gordon, G.G.; Olivo, J.; Rafii, F.; and Southren, A.L. Conversion of androgens to estrogens in cirrhosis of the liver. Journal of Clinical Endocrinology and Metabolism 40:1018-1026, 1975.

Gordon, G.G., and Southren, A.L. Metabolic effects of alcohol on the endocrine system. In: Lieber, C.S., ed. Metabolic Aspects of Alcoholism. Baltimore: University Park Press, 1977. pp. 249-302.

Gordon, G.G.; Southren, A.L.; and Lieber, C.S. Hypogonadism and feminization in the male: A triple effect of alcohol. Alcoholism: Clinical and Experimental Research 3:210-212, 1979.

Gottfried, E.B.; Korsten, M.A.; and Lieber, C.S. Gastritis and duodenitis induced by alcohol: An endoscopic and histologic assessment (abstract). Gastroenterology 70:A-32/890, 1976.

Gould, L.; Shariff, M.; Zahir, M.; and Di Lieto, M. Cardiac hemodynamics in alcoholic patients with chronic liver disease and a presystolic gallop. Journal of Clinical Investigation 48:860-868, 1969.

Gould, L.; Zahir, M.; DeMartino, A.; and Gomprecht, R.F. Cardiac effects of a cocktail. Journal of the American Medical Association 218:1799-1802, 1971.

Greenspon, A.J.; Leier, C.V.; and Schaal, S.F. Acute ethanol effects cardiac arrhythmias and conduction in man (abstract). Clinical Research 29:200A, 1981.

Halle, P.; Pare, P.; Kaptein, E.; Kanel, G.; Redeker, A.G.; and Reynolds, T.B. Double-blind, controlled trial of propylthiouracil in patients with severe acute alcoholic hepatitis. Gastroenterology 82:925-931, 1982.

Halsted, C.H.; Griggs, R.C.; and Harris, J.W. The effect of alcoholism on the absorption of folic (H^3PGA) evaluated by plasma levels and urine excretion. Journal of Laboratory and Clinical Medicine 69:116-131, 1967.

Halsted, C.H.; Robles, E.A.; and Mezey, E. Intestinal malabsorption in folate-deficient alcoholics. Gastroenterology 64:526-532, 1973.

Hed, R.; Lundmark, C.; Fahlgren, H.; and Orell, S. Acute muscular syndrome in chronic alcoholism. Acta Medica Scandinavica 171:585-599, 1962.

Helderman, J.H.; Vestal, R.E.; Rowe, J.W.; Tobin, J.; Andres, R.; and Robertson, G. The response of arginine vasopressin to intravenous ethanol and hypertonic saline in man: The impact of aging. Journal of Gerontology 33:39-47, 1978.

Hines, J.D., and Cowan, D.H. Anemia in alcoholism. In: Dimitrov, N.V., and Nodine, J.H., eds. Drugs and Hematologic Reactions. New York: Grune & Stratton, 1974. pp. 141-153.

Hion-Jon, V. The influence of alcohol on the endocrine glands. Folia Neuropathologica Estoniana 3:288-301, 1925.

Hogan, W.J.; Viegas De Andrade, S.R.; and Winship, D.H. Ethanol induced acute esophageal motor dysfunction. Journal of Applied Physiology 32: 755-760, 1972.

Hoyumpa, A.M.; Breen, K.J.; and Schenker, S. Thiamine transport across the rat intestine: II. Effect of ethanol. Journal of Laboratory and Clinical Medicine 86:803-816, 1975.

Hoyumpa, A.; Middleton, H.; Wilson, F.; and Schenker, S. Dual system of thiamine transport: Characteristics and effect of ethanol (abstract). Gastroenterology 66:A-60/714, 1974.

Hoyumpa, A.M.; Nichols, S.G.; Wilson, F.A.; and Schenker, S. Effect of ethanol on interstitial (Na,K) ATPase and intestinal thiamine transport in rats. Journal of Laboratory and Clinical Medicine 90:1086-1095, 1977.

Ibrahim, N.G.; Spieler, P.J.; and Freedman, M.L. Ethanol inhibition of rabbit reticulocyte haem synthesis at the level of delta-aminolaevulinic acid synthetase. British Journal of Haematology 41:235-243, 1979.

Israel, Y.; Salazar, L.; and Rosenmann, E. Inhibitory effects of alcohol on intestinal amino acid transport in vivo and in vitro. Journal of Nutrition 96:499-504, 1968.

Israel, Y.; Videla, L.; MacDonald, A.; and Bernstein, J. Metabolic alteration produced in the liver by chronic ethanol administration. Biochemical Journal 134:523-529, 1973.

Israel, Y.; Walfish, P.G.; Orrego, H.; Blake, J.; and Kalant, H. Thyroid hormones in alcoholic liver disease. Effect of treatment with 6-n-propylthiouracil. Gastroenterology 76:116-122, 1979.

Jeffcoate, W.J.; Herbert, M.; Cullen, M.H.; Hasting, A.G.; and Walder, C.P. Prevention of effects of alcohol intoxication by naloxone. Lancet 2: 1157-1159, 1979.

Jefferys, D.B.; Flanagan, R.J.; and Volans, G.N. Reversal of ethanol-induced coma with naloxone (letter). Lancet 1:308-309, 1980.

Jones, J.E.; Shane, S.R.; Jacob, W.H.; and Flink, E.B. Magnesium balance studies in chronic alcoholism. Annals of the New York Academy of Sciences 162:934-946, 1969.

Jung, Y., and Russfield, A.B. Prolactin cells in the hypophysis of cirrhotic patients. Archives of Pathology 94:265-269, 1972.

Kalbfleisch, J.J.; Lindeman, R.D.; Ginn, H.E.; and Smith, W.O. Effects of ethanol administration on urinary excretion of magnesium and other electrolytes in alcoholic and normal subjects. Journal of Clinical Investigation 42:1471-1475, 1963.

Karasawa, T.; Kushida, T.; Shikata, T.; and Kaneda, H. Morphologic spectrum of liver diseases among chronic alcoholics: A comparison between Tokyo, Japan, and Cincinnati, U.S.A. Acta Pathologica Japonica 30:505-514, 1980.

Kershenobich, D.; Fierro, F.J.; and Rojkind, M. The relationship between the free pool of proline and collagen content in human liver cirrhosis. Journal of Clinical Investigation 49:2246-2249, 1970.

Kjellen, G., and Tibbling, L. Influence of body position, dry and water swallows, smoking and alcohol on esophageal acid clearing. Scandinavian Journal of Gastroenterology 13:283-288, 1978.

Klatsky, A. "The Kaiser-Permanente Experience." Paper presented at the symposium on Alcohol and Cardiovascular Disease of the 20th Annual Conference on Cardiovascular Epidemiology, San Diego, 1980.

Knochel, J.P. The pathophysiology and clinical characteristics of severe hypophosphatemia. Archives of Internal Medicine 137:203-220, 1977.

Krawitt, E.L. Ethanol inhibits intestinal calcium transport in rats. Nature 243:88-89, 1973.

Krawitt, E.L. Effect of ethanol ingestion on duodenal calcium transport. Journal of Laboratory and Clinical Medicine 85:665-671, 1975.

Krebs, H.A.; Hems, R.; and Lund, P. Accumulation of amino acids by the perfused rat liver in the presence of ethanol. Biochemical Journal 134: 697-705, 1973.

Kreisberg, R.A.; Owen, W.C.; and Siegal, A.M. Hyperlacticacidemia in man: Ethanol-phenformin synergism. Journal of Clinical Endocrinology and Metabolism 34:29-35, 1972.

Kuhl, C., and Anderson, O. Glucose- and tolbutamide-mediated insulin response after preinfusion with ethanol. Diabetes 23:821-826, 1974.

Kuo, Y.-J., and Shanbour, L.L. Effects of ethanol on sodium, 3-0-methyl glucose, and L-alinine transport in the jejunum. American Journal of Digestive Diseases 123:51-56, 1978.

Lane, F.; Goff, P.; McGuffin, R.; Eichner, E.R.; and Hillman, R.S. Folic acid metabolism in normal, folate deficient and alcoholic man. British Journal of Haematology 34:489-500, 1976.

Larato, D.C. Oral tissue changes in the chronic alcoholic. Journal of Periodontology 43:772-773, 1972.

Laversen, N.H.; Raghavan, K.S.; Wilson, K.H.; Fuchs, F.; and Niemann, W.H. Effects of prostaglandin F_{2alpha}oxytocin, and ethanol on the uterus of the pregnant baboon. American Journal of Obstetrics and Gynecology 115:912-918, 1973.

Leevy, C.M.; Baker, H.; Ten Hove, W.; Frank, O.; and Cherrick, G.R. B-complex vitamins in liver disease on the alcoholic. American Journal of Clinical Nutrition 16:339-346, 1965.

Lefevre, A.; Adler, H.; and Lieber, C.S. Effect of ethanol on ketone metabolism. Journal of Clinical Investigation 49:1775-1782, 1970.

Leier, C.V.; Schaal, S.F.; Leighton, R.F.; and Whayne, T.F. Heart block in alcoholic cardiomyopathy. Archives of Internal Medicine 134: 766-768, 1974.

Lemon, F.R.; Walden, R.T.; and Woods, R.W. Cancer of the lung and mouth in Seventh-Day Adventists. Cancer 17:486-497, 1964.

Liang, C.S., and Lowenstein, J.M. Metabolic control of the circulation: Effects of acetate and pyruvate. Journal of Clinical Investigation 62 (5):1029-1038, 1978.

Lieber, C.S. Chronic alcoholic hepatic injury in experimental animals and man: Biochemical pathways and nutritional factors. Federation Proceedings 26:1443-1448, 1967.

Lieber, C.S. Alcohol and the liver. In: Bittar, E.E., and Bittar, N., eds. The Biological Basis of Medicine. Vol. 5. New York: Academic Press, 1969. pp. 317-344.

Lieber, C.S. Pathogenesis of alcoholic liver disease: An overview. In: Fisher, M.M., and Rankin, J.G., eds. Alcohol and the Liver. Hepatology: Research and Clinical Issues, Vol. 3. New York: Plenum Press, 1977. pp. 197-255.

Lieber, C.S. Metabolic effects of ethanol on the liver and other digestive organs. In: Leevy, C.M., ed. Alcohol and the GI Tract. Clinics in Gastroenterology, Vol. 10, No. 2. London: W.B. Saunders, 1981. pp 315-342.

Lieber, C.S., and DeCarli, L.M. Study of agents for the prevention of the fatty liver produced by prolonged alcohol intake. Gastroenterology 50: 316-322, 1966.

Lieber, C.S., and DeCarli, L.M. Ethanol oxidation by hepatic microsomes. Adaptive increase after ethanol feeding. Science 162:917-918, 1968.

Lieber, C.S.; Jones, D.P.; and DeCarli, L.M. Effects of prolonged ethanol intake: Production of fatty liver despite adequate diet. Journal of Clinical Investigation 44:1009-1021, 1965.

Lieber, C.S.; Seitz, H.K.; Garro, A.J.; and Worner, T.M. Alcohol-related diseases and carcinogenesis. Cancer Research 39:2863-2886, 1979.

Lieber, C.S., and Spritz, N. Effects of prolonged ethanol intake in man: Role of dietary, adipose, and endogenously synthesized fatty acids in the pathogenesis of the alcoholic fatty liver. Journal of Clinical Investigation 45:1400-1411, 1966.

Linkola, J.; Fyhrquist, F.; and Forsander, O. Effects of ethanol in urinary arginine vasopressin excretion in two rat strains selected for their different ethanol preferences. Acta Physiologica Scandinavica 101:126-128, 1977.

Liu, Y.K. Leukopenia in alcoholics. American Journal of Medicine 54:605-610, 1973.

Lochner, A.; Cowley, R.; and Brink, A.J. Effects of ethanol on metabolism and function of perfused rat heart. American Heart Journal 78:770-780, 1969.

Longacre, A.M., and Popky, G.L Papillary necrosis in patients with cirrhosis: A study of 102 patients. Journal of Urology 99:391-395, 1968.

Loosen, P.T., and Prange, A.J. Alcohol and anterior pituitary secretion. Lancet 2:985, 1977.

Louria, D.B. Susceptibility to infection during experimental alcohol intoxication. Transactions of the Association of American Physicians 76:102-112, 1963.

Lue, S.L.; Paronetto, F.; and Lieber, C.S. Cytotoxicity of lymphocytes in alcoholic fatty liver: Respective role of lymphocytes and target cells (abstract). Gastroenterology 76:1290, 1979.

Lumeng, L., and Li, T.-K. Vitamin B_6 metabolism in chronic alcohol abuse: Pyridoxal phosphate levels in plasma and the effects of acetaldehyde on pyridoxal phosphate synthesis and degradation in human erythrocytes. Journal of Clinical Investigation 53:693-704, 1974.

Lyon, J.L.; Klauber, M.R.; Gardner, J.W.; and Smart, C.R. Cancer incidence in Mormons and non-Mormons in Utah, 1966-1970. New England Journal of Medicine 294:129-133, 1976.

MacGregor, R.R.; Spagnuolo, P.J.; and Lentnek, A.L. Inhibition of granulocyte adherence by ethanol, prednisone and aspirin, measured with an assay system. New England Journal of Medicine 291:642-646, 1974.

Main, I.H.M., and Whittle, B.J.R. The role of prostaglandins in gastric acid secretion. In: Case, R.J., and Goebell, H., eds. Stimulus-Secretion Coupling in the Gastrointestinal Tract. Baltimore: University Park Press, 1976. pp. 147-157.

Marco, J.; Diego, J.; Villanueva, M.L.; Diaz-Fierros, M.; Valverde, I.; and Segovia, J.M. Elevated plasma glucagon levels in cirrhosis. New England Journal of Medicine 289:1107-1111, 1973.

Marks, V., and Medd, W.E. Alcohol induced hypoglycemia. British Journal of Psychiatry 110:228-232, 964.

Marquis, C.; Marchetti, J.; Burlet, C.; and Boulande, M. Secretion urinaire et hormone antidiuretique chez des rats soumis a une administration repetee d'ethanol [Urinary secretion and antidiuretic hormone in rats subjected to repeated ethanol administration]. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 169:154-161, 1975.

Martin, J.L.; Justus, P.G.; and Mathias, J.R. Altered motility of the small intestine in response to ethanol (ETOH): An explanation for the diarrhea associated with the consumption of alcohol (abstract). Gastroenterology 78:1218, 1980.

Martin, S., and Pangborn, R.M. Human parotid secretion in response to ethyl alcohol. Journal of Diet Research 50:485-490, 1971.

Martini, G.A., and Wienbeck, M. Beguenstigt Alkohol die Entstehung eines Barrett-Syndroms (Endobrachyoesophagus) [Does alcohol promote the development of Barrett's syndrome (endobrachy-esophagus)]. Deutsche Medizinische Wochenschrift 99:434-439, 1974.

Matsuda, Y.; Baraona, E.; Salaspuro, M.; and Lieber, C.S. Effects of ethanol on liver microtubules and Golgi apparatus: Possible role in altered hepatic secretion of plasma proteins. Laboratory Investigation 41:455-463, 1979.

Matsuzaki, S.; Gordon, E.; and Lieber, C.S. Increased alcohol dehydrogenase independent ethanol oxidation at high ethanol concentrations in isolated rat hepatocytes: The effect of chronic ethanol feeding. Journal of Pharmacology and Experimental Therapeutics 217:133-137, 1981.

Mayer, E.M.; Grabowski, C.J.; and Fisher, R.S. Effects of graded doses of alcohol upon esophageal motor function. Gastroenterology 75:1133-1136, 1978.

McCoy, G.D., and Wynder, E.L. Etiological and preventive implications in alcohol carcinogenesis. Cancer Research 39:2844-2850, 1979.

McGlashan, N.D.; Walters, C.L.; and McLean, A.E.M. Nitrosamines in African alcoholic spirits and esophageal cancer. Lancet 2:1017, 1968.

Mezey, E. Ethanol: Metabolism and adverse effects. Viewpoints on Digestive Diseases 11:215-219, 1979.

Middleton, W.R.J.; Carter, E.A.; Drummey, G.D.; and Isselbacher, K.J. Effect of oral ethanol administration on intestinal cholesterogenesis in the rat. Gastroenterology 60:880-887, 1971.

Moore, M.R. The effects of ethanol on heme biosynthesis (abstract). In: Thurman, R.G.; Yonetani, T.; Williamson, J.R.; and Chance, B., eds. Alcohol and Aldehyde Metabolizing Systems. New York: Academic Press, 1974. p. 543.

Morgan, M.Y., and Sherlock, S. Sex-related differences among 100 patients with alcoholic liver disease. British Medical Journal 1:939-941, 1977.

Morin, J., and Porte, P. Macrocytose erythrocytaire chez les ethyliques [Erythrocyte macrocytosis in alcoholics] (letter). Nouvelle Presse Medicale 5:273, 1976.

Morland, J.; Bessesen, A.; and Svendsen, L. Incorporation of labelled amino acids into proteins of isolated parenchymal and nonparenchymal rat liver cells in the absence and presence of ethanol. Biochimica et Biophysica Acta 561:464-474, 1979.

Morley, J.E.; Baranetsky, N.G.; Wingert, T.D.; Carlson, H.E.; Hershman, J.M.; Melmed, S.; Levin, S.R.; Jamison, K.R.; Weitzman, R.; Chang, R.S.; and Varner, A.A. Endocrine effects of naloxone-induced opiate receptor blockade. Journal of Clinical Endocrinology and Metabolism 50:251-257, 1980.

Murray, J., and Stein, N. Effect of ethanol on absorption of iron in rats. Proceedings of the Society for Experimental Biology and Medicine 120:816-819, 1965.

Nakamura, K.; Sarles, H.; and Payan, H. Three-dimensional reconstruction of the pancreatic ducts in chronic pancreatitis. Gastroenterology 62:942-949, 1972.

Nakano, J., and Moore, S.E. Effects of different alcohols on the contractile force of the isolated guinea pig myocardium. European Journal of Pharmacology 20:266-270, 1972.

Newman, W.H., and Valicenti, J.F. Ventricular function following acute alcohol administration: A strain-gauge analysis of depressed ventricular dynamics. American Heart Journal 81:61-68, 1971.

Nilsson, B.E. Conditions contributing to fracture of the femoral neck. Acta Chirurgica Scandinavica 136:383-384, 1970.

Noble, E.P.; Kakihana, R.; and Butte, J.C. Corticosterone metabolism in alcohol-adapted mice. In: Roach, M.K.; McIssac, W.M.; and Creaven, P.J., eds. Biological Aspects of Alcohol. Advances in Mental Science III. Dallas: University of Texas Press, 1971. pp. 389-417.

Olivo, J.; Gordon, G.G.; Rafii, F.; and Southren, A.L. Estrogen metabolism in hyperthyroidism and in cirrhosis of the liver. Steroids 26:47-56, 1975.

Ono, J.; Hutson, D.G.; and Dombro, R.S. Tryptophan and hepatic coma. Gastroenterology 74: 196-200, 1978.

Orrego, H.; Kalant, H.; Israel, Y.; Blake, J.; Medline, A.; Rankin, J.G.; Armstrong, M.; and Kapur, B. Effect of short-term therapy with propylthiouracil in patients with alcoholic liver disease. Gastroenterology 76:105-115, 1979.

Oxenkrug, G.F. Dexamethasone test in alcoholics (letter). Lancet 2:795, 1978.

Paronetto, F., and Lieber, C.S. Cytotoxicity of lymphocytes in experimental alcoholic liver injury in the baboon. Proceedings of the Society for Experimental Biology and Medicine 153:495-497, 1976.

Pekkanen, L.; Eriksson, K.; and Shivonen, M.-L. Dietarily-induced changes in voluntary ethanol consumption and ethanol metabolism in the rat. British Journal of Nutrition 40:103-113, 1978.

Peng, T.C.; Cooper, G.W.; and Munson, P.L. The hypocalcemic effect of ethyl alcohol in rats and dogs. Endocrinology 91:586-593, 1972.

Peng, T.C., and Gitelman, H.J.L. Ethanol-induced hypocalcemia, hypermagnesemia and inhibition of the serum calcium-raising effect of parathyroid hormone in rats. Endocrinology 94:608-611, 1974.

Perin, A., and Sessa, A. In vitro effects of ethanol and acetaldehyde on tissue protein synthesis. In: Lindros, K.O., and Eriksson, C.J.P., eds. The Role of Acetaldehyde in the Actions of Ethanol. Helsinki: The Finnish Foundation for Alcohol Studies, 1975. pp. 105-122.

Perlow, W.; Baraona, E.; and Lieber, C.S. Symptomatic intestinal disaccharidase deficiency in alcoholics. Gastroenterology 68:935-942, 1975.

Phaosawasdi, K.; Tolin, R.; Mayer, E.; and Fisher, R.S. Effects of alcohol on the pyloric sphincter. Digestive Diseases and Sciences 24:934-939, 1979.

Phillips, G.B., and Safrit, H.F. Alcoholic diabetes: Induction of glucose intolerance with alcohol. Journal of the American Medical Association 217:1513-1519, 1971.

Phillips, R.L. Cancer among Seventh-Day Adventists. Journal of Environmental Pathology and Toxicology 3:157-169, 1980.

Pickrell, K.L. The effect of alcoholic intoxication and ether anaesthesia on resistance to pneumococcal infection. Bulletin of the Johns Hopkins Hospital 63:238-260, 1938.

Pirola, R.C., and Davis, A.E. Effect of intravenous alcohol on motility of the duodenum and of the sphincter of Oddi. Australian Annals of Medicine 19:24-29, 1970.

Pirola, R.C., and Lieber, C.S. [illegible]nergy cost of the metabolism of drugs, [illegible]ding ethanol. Pharmacology 7:185-196, 1972.

Pohorecky, L.A. Effects of ethanol on central and peripheral noradrenergic neurons. Journal of Pharmacology and Experimental Therapeutics 189:380-391,1974.

Popper, H., and Lieber, C.S. Histogenesis of alcoholic fibrosis and cirrhosis in the baboon. American Journal of Pathology 98:695-716, 1980.

Rachamin, G.; MacDonald, J.A.; Wahid, S.; Clapp, J.J.; Khanna, J.M.; and Israel, Y. Modulation of alcohol dehydrogenase and ethanol metabolism by sex hormones in the spontaneously hypertensive rat. Biochemical Journal 186:483-490, 1980.

Raiha, N. Effect of ethanol on cytological changes induced by salt load in nucleus supraopticus of rat. Proceedings of the Society for Experimental Biology and Medicine 103:387-391, 1960.

Rankin, J.G.; Hale, G.S.; Wilkinson, P.; O'Day, D.M.; Santamaria, J.N.; and Babarczy, G. Relationship between smoking and pulmonary disease in alcoholism. Medical Journal of Australia 1:730-733, 1969.

Rasmussen, H. Parathyroid hormone, calcitonin, and the calciferols. In: Williams, R.H., ed. Textbook of Endocrinology, 5th ed. Philadelphia: W.B. Saunders Co., 1974. p. 680-773.

Reber, H.A. Chronic pancreatitis. In: Sleisenger,

M.H., and Fordtran, J.S., eds. Gastrointestinal Disease: Pathophysiology, Diagnosis, Management. Philadelphia: W.B. Saunders Co., 1978. pp. 1439-1456.

Redmond, G.P. Effect of ethanol on endogenous rhythms of growth hormone secretion. Alcoholism: Clinical and Experimental Research 4:50-56, 1980.

Regan, T.J.; Levinson, G.E.; Oldewurtel, H.A.; Frank, M.J.; Weisse, A.B.; and Moschos, C.B. Ventricular function in noncardiacs with alcoholic fatty liver: Role of ethanol in the production of cardiomyopathy. Journal of Clinical Investigation 48:397-407, 1969.

Robert, A.; Nezamis, J.E.; Hanchar, A.J.; and Lancaster, C. Aspirin combined with alcohol is ulcerogenic (abstract). Gastroenterology 78(5, part 2):1245, 1980.

Rodgers, J.B., and O'Brien, R.J. The effect of acute ethanol treatment on lipid-reesterifying enzymes of the rat small bowel. American Journal of Digestive Diseases 20(4):354-358, 1975.

Rojkind, M., and DeLeon, L.D. Collagen biosynthesis in cirrhotic rat liver slices: A regulatory mechanism. Biochimica et Biophysica Acta 217: 512-522, 1970.

Rosen, H.M.; Yoshimura, N.; Hodgman, J.M.; and Fischer, J.E. Plasma amino acid patterns in hepatic encephalopathy of differing etiology. Gastroenterology 72:483-487, 1977.

Rosenberg, L.; Slone, D.; Shapiro, S.; Kaufman, D.W.; Helmrich, S.P.; Miettinen, O.S.; Stolley, P.D.; Levy, M.; Rosenshein, N.B.; Schottenfeld, D.; and Engle, R.L., Jr. Breast cancer and alcoholic-beverage consumption. Lancet 1:267-271, 1982.

Rothman, K.J. The proportion of cancer attributable to alcohol consumption. Preventive Medicine 9:174-179, 1980.

Rothman, K., and Keller, A. The effect of joint exposure to alcohol and tobacco on risk of cancer of the mouth and pharynx. Journal of Chronic Diseases 25:711-716, 1972.

Rubin, E.; Rybak, B.J.; Lindenbaum, J.; Gerson, C.D.; Walker, G.; and Lieber, C.S. Ultrastructural changes in the small intestine induced by ethanol. Gastroenterology 63:801-814, 1972.

Rudman, D.; Sewell, D.W.; and Ansley, J.D. Deficiency of carnitine in cachectic cirrhotic patients. Journal of Clinical Investigation 60:716-723, 1977.

Salaspuro, M., and Lieber, C.S. Non-uniformity of blood ethanol elimination: Its exaggeration after chronic consumption. Annals of Clinical Research 10:294-297, 1978.

Sanchez-Calvo, R. Die Alkoholvergiftung und ihre Folgen fuer das endokrine und das Ernaehrungssystem [Alcohol intoxication and its consequences for the endocrine and nutrition system]. Virchows Archiv 308:14-21, 1941.

Sarles, H. Chronic calcifying pancreatitis-chronic alcoholic pancreatitis. Gastroenterology 66:604-616, 1974.

Sarles, H. Alcohol and the pancreas. In: Seixas, F.A.; Williams, K.; and Eggleston, S., eds. Medical Consequences of Alcoholism. Annals of the New York Academy of Sciences, Vol. 252, 1975. pp. 171-182.

Saville, P.D., and Lieber, C.S. Effect of alcohol on growth, bone density and muscle magnesium in the rat. Journal of Nutrition 87:477-484, 1965.

Schottenfeld, D. Alcohol as a co-factor in the etiology of cancer. Cancer 43:1962-1966, 1979.

Schreiber, S.S.; Briden, K.; Oratz, M.; and Rothschild, M.A. Ethanol, acetaldehyde, and myocardial protein synthesis. Journal of Clinical Investigation 51:2808-2826, 1972.

Schreiber, S.S.; Oratz, M.; and Rothschild, M.A. Alcoholic cardiomyopathy. II. The inhibition of cardiac microsomal protein synthesis by acetaldehyde. Journal of Molecular and Cellular Cardiology 6:207-213, 1974.

Seitz, H.K.; Garro, A.J.; and Lieber, C.S. Enhanced pulmonary and intestinal activation of procarcinogens and mutagens after chronic ethanol consumption in the rat. European Journal of Clinical Investigation 11:33-38, 1981a.

Seitz, H.K.; Garro, A.J.; and Lieber, C.S. Sex dependent effect of chronic ethanol consumption in rats on hepatic microsome mediated mutagenicity of benzo(a)pyrene. Cancer Letters 13:97-102, 1981b.

Shah, J.H.; Wongsurawat, N.; and Aran, P.P. Effect of ethanol on stimulus-induced insulin secretion and glucose tolerance: A study of mechanisms. Diabetes 26:271-277, 1977.

Shaw, S., and Lieber, C.S. Plasma amino acid abnormalities in alcoholics. Gastroenterology 74: 677-682, 1978.

Shaw, S.; Stimmel, B.; and Lieber, C.S. Plasma alpha amino-n-butyric acid to leucine ratio: An empirical biochemical marker of alcoholism. Science 196:1057-1058, 1976.

Shirazi, S.S., and Platz, C.E. Effect of alcohol on canine esophageal mucosa. Journal of Surgical Research 25:373-379, 1978.

Singh, S.P., and Patel, D.G. Effects of ethanol on carbohydrate metabolism. I. Influence on oral glucose tolerance test. Metabolism 25:239-243, 1976.

Smith, J.J. The effect of alcohol on adrenal ascorbic acid and cholesterol of the rat (abstract). Journal of Clinical Endocrinology 11:792, 1951.

Sorrell, M.F.; Nauss, J.M.; Donahue, T.M.; and Tuma, D.J. Effects of chronic ethanol administration on hepatic glycoprotein secretion in the rat. Gastroenterology 84:580-586, 1983.

Southren, A.L.; Gordon, G.G.; Olivo, J.; Rafii, F.; and Rosenthal, W.S. Androgen metabolism in cirrhosis of the liver. Metabolism Clinical and Experimental 22:695-702, 1973.

Spann, J.F., Jr.; Mason, D.T.; Beiser, G.D.; and Gold, H.K. Actions of ethanol on the contractile state of the normal and failing cat papillary muscle (abstract). Clinical Research 16:249, 1968.

Spiegelholder, B.; Eisenbrand, G.; and Preussmann,

R. Contamination of beer with trace quantities of N-nitrosodimethylamine. Food and Cosmetics Toxicology 17:29-31, 1979.

Sporn, M.B.; Dunlop, N.M.; Newton, D.L.; and Smith, J.M. Prevention of chemical carcinogenesis by vitamin A and its synthetic analogs (retinoids). Federation Proceedings 35(6):1332-1338, 1976.

Stokes, P.E. Adrenocortical activity in alcoholics during chronic drinking. In: Seixas, F.A., and Eggleston, S., eds. Alcoholism and the Central Nervous System. Annals of the New York Academy of Sciences, Vol. 215, 1973. pp. 77-83.

Strum, W.B., and Spiro, H.M. Chronic pancreatitis. Annals of Internal Medicine 74:264-277, 1971.

Sullivan, J.F. Effect of alcohol on urinary zinc excretion. Quarterly Journal of Studies on Alcohol 23:216-220, 1962.

Sullivan, L.W., and Herbert, V. Suppression of hematopoiesis by ethanol. Journal of Clinical Investigation 43:2048-2062, 1964.

Swartz, M.H.; Repke, D.I.; Katz, A.M.; and Rubin, E. Effects of ethanol on calcium binding and calcium uptake by cardiac microsomes. Biochemical Pharmacology 23:2369-2376, 1974.

Tabakoff, B.; Jaffe, R.C.; and Ritzmann, R.F. Corticosterone concentrations in mice during ethanol drinking and withdrawal. Journal of Pharmacy and Pharmacology 30: 371-374, 1978.

Tapper, E.J.; Bushi, S.; Ruppert, R.D.; and Greenberger, N.J. Effect of acute and chronic ethanol treatment on the absorption of iron in rats. American Journal of the Medical Sciences 255: 46-52, 1968.

Thomson, A.D.; Baker, H.; and Leevy, C.M. Patterns of ^{35}S-thiamine hydrochloride absorption in the malnourished alcoholic patient. Journal of Laboratory and Clinical Medicine 76:34-45, 1970.

Torro, G.; Kolodny, R.C.; Jacobs, L.S.; and Masters, W.H. Failure of alcohol to alter pituitary and target organ hormone levels (abstract). Clinical Research 21:505, 1973.

Tuyns, A.J. Alcohol and cancer. Alcohol Health and Research World 2:20-31, 1978.

Tuyns, A.J. Epidemiology of alcohol and cancer. Cancer Research 39:2840-2843, 1979.

Tuyns, A.J. Alcohol. In: Schottenfeld, D., and Fraumeni, J.F., Jr., eds. Cancer Epidemiology and Prevention. Philadelphia: W.B. Saunders Co., 1982. pp. 293-303.

Unger, K.W., and Johnson, D. Red blood cell mean corpuscular volume: A potential indicator of alcohol usage in a working population. American Journal of the Medical Sciences 267:281-289, 1974.

Van Thiel, D.H. Alcohol and its effect upon endocrine function. Alcoholism: Clinical and Experimental Research 4:44-49, 1980.

Van Thiel, D.H. Adrenal response to ethanol: A stress response? In: Pohorecky, L.A., and Brick, J., eds. Stress and Alcohol Use. New York: Elsevier Biomedical, 1983a. pp. 23-27.

Van Thiel, D.H. Ethanol: Its adverse effects upon the hypothalamic-pituitary-gonadal axis. Journal of Laboratory and Clinical Medicine 101: 21-33, 1983b.

Van Thiel, D.H., and Lester, R. Alchoholism: Its effect on hypothalamic-pituitary-gonadal function. Gastroenterology 71:318-327, 1976a.

Van Thiel, D.H., and Lester, R. Sex and alcohol: A second peek (editorial). New England Journal of Medicine 295:835-836, 1976b.

Van Thiel, D.H., and Lester, R. The effect of chronic alcohol abuse on sexual function. Clinics in Endocrinology and Metabolism 8:499-510, 1979a.

Van Thiel, D.H., and Lester, R. Hypothalamic-pituitary-gonadal dysfunction in patients with alcoholic liver disease. In: Davidson, C.S., ed. Problems in Liver Disease. New York: Stratton Intercontinental Medical Book Corp., 1979b. pp.286-298.

Van Thiel, D.H.; Gavaler, J.S.; and Lester, R. Ethanol inhibition of vitamin A metabolism in the testes: Possible mechanism for sterility in alcoholics. Science 186:941-942, 1974a.

Van Thiel, D.H.; Lester, R.; and Sherins, R.J. Hypogonadism in alcoholic liver disease: Evidence for a double defect. Gastroenterology 67:1188-1199, 1974b.

Van Thiel, D.H.; Gavaler, J.S.; Lester, R.; and Goodman, M.D. Alcohol-induced testicular atrophy: An experimental model for hypogonadism occurring in chronic alcoholic men. Gastroenterology 69:326-332, 1975a.

Van Thiel, D.H.; Gavaler, J.S.; Lester, R.; Loriaux, D.L.; and Braunstein, G.D. Plasma estrone, prolactin, neurophysin and sex steroid-binding globulin in chronic alcoholic men. Metabolism 24: 1015-1019, 1975b.

Van Thiel, D.H.; Gavaler, J.S.; Little, J.M.; and Lester, R. Alcohol: Its effect on the kidney. Metabolism 26:857-866, 1977.

Van Thiel, D.H.; Gavaler, J.S.; Lester, R.; and Sherins, R.J. Alcohol-induced ovarian failure in the rat. Journal of Clinical Investigation 61: 624-632, 1978a.

Van Thiel, D.H.; Gavaler, J.S.; Wight, C.; Smith, W.I.; and Abuid, J. Thyrotropin-releasing hormone (TRH)-induced growth hormone (hGH) responses in cirrhotic men. Gastroenterology 75: 66-70, 1978b.

Van Thiel, D.H.; Lester, R.; and Vaitukaitis, J. Evidence for a defect in pituitary secretion of luteinizing hormone in chronic alcoholic men. Journal of Clinical Endocrinology and Metabolism 47:499-507, 1978c.

Van Thiel, D.H.; McClain, C.J.; Elson, M.K.; and McMillin, M.J. Hyperprolactinemia and thyrotropin-releasing factor responses in men with alcoholic liver disease. Alcoholism: Clinical and Experimental Research 2:344-348, 1978d.

Van Thiel, D.H.; Gavaler, J.S.; Cobb, C.F.; Sherins, R.J.; and Lester, R. Alcohol induced testicular atrophy in the adult male rat. Endocrinology 105:888-895, 1979a.

Van Thiel, D.H.; Smith, W.I.; Wight, C.; and Abuid, J. Elevated basal and abnormal thyrotropin-

releasing hormone-induced thyroid-stimulating hormone secretion in chronic alcoholic men with liver disease. Alchoholism: Clinical and Experimental Research 3:302-308, 1979b.

Van Thiel, D.H.; Gavaler, J.S.; Slone, F.L.; Cobb, C.F.; Smith, W.I.; Klaus, M.B.; and Lester, R. Is feminization in alcoholic men due in part to portal hypertension: A rat model. Gastroenterology 78:81-91, 1980.

Veitch, R.L.; Lumeng, L.; and Li, T.-K. Vitamin B_6 metabolism in chronic alcohol abuse: The effect of ethanol oxidation on hepatic pyridoxal 5'-phosphate metabolism. Journal of Clinical Investigation 55:1026-1032, 1975.

Verdy, M., and Caron, D. Ethanol et absorption du calcium chez l'humain [Ethanol and calcium absorption in man]. Biologie et Gastroenterologie 6:157-160, 1973.

Wagner, G., and Fuchs, A.-R. Effects of ethanol on uterine activity during suckling in post-partum women. Acta Endocrinologica 58:133-141, 1968.

Walsh, M.J., and Truitt, E.B. Acetaldehyde mediation in the mechanism of ethanol-induced changes in norepinephrine metabolism. Molecular Pharmacology 6:416-424, 1970.

Wang, J., and Pierson, R.N. Distribution of zinc in skeletal muscle and liver tissue in normal and dietary controlled alcoholic rats. Journal of Laboratory and Clinical Medicine 85:50-58, 1975.

Wehman, H.J., and Plantholt, B.A. Asbestos fibrils in beverages. I. Gin. Bulletin of Environmental Contamination and Toxicology 11:267-272, 1974.

Weinstein, M.J., and Deykin, D. Quantitative abnormality of an alpha-chain molecular weight form in the fibrinogen of cirrhotic patients. British Journal of Haematology 40:617-630, 1978.

Whitehead, T.P.; Clarke, C.A.; and Whitfield, A.G.W. Biochemical and haematological markers of alcohol intake. Lancet 1:978-981, 1978.

Wilkinson, P.; Santamaria, J.N.; and Rankin, J.G. Epidemiology of alcoholic cirrhosis. Australian Annals of Medicine 18:222-226, 1969.

Williams, G.A.; Bowser, E.N.; Hargis, G.K.; Kukreja, S.C.; Shah, J.H.; Vora, N.M.; and Henderson, W.J. Effect of ethanol on parathyroid hormone and calcitonin secretion in man. Proceedings of the Society for Experimental Biology and Medicine 159:187-191, 1978.

Williams, J.W.; Tada, M.; Katz, A.M.; and Rubin, E. Effects of ethanol and acetaldehyde on the ($Na^+ + K^+$)-activated adenosine triphosphatase activity of cardiac plasma membranes. Biochemical Pharmacology 24:27-32, 1975.

Williams, R.R., and Horm, J.W. Association of cancer sites with tobacco and alcohol consumption and socioeconomic status of patients: Interview study from the Third National Cancer Survey. Journal of the National Cancer Institute 58:525-547, 1977.

Winship, D.H.; Caflisch, C.R.; Zboralske, F.F.; and Hogan, W.J. Deterioration of esophageal peristalsis in patients with alcoholic neuropathy. Gastroenterology 55:173-178, 1968.

Winsor, A.L., and Strongin, E.I. The effect of alcohol on the rate of parotid secretion. Journal of Experimental Psychology 16:589-597, 1933.

Wright, J.; Merry, J.; Fry, D.; and Marks, V. Pituitary function in chronic alcoholism. In: Gross, M.M., ed. Alcohol Intoxication and Withdrawal. II. Advances in Experimental Medicine and Biology, Vol. 59, 1975. pp. 253-255.

Wright, J.W. Endocrine effects of alcohol. In: Marks, V., and Wright, H., eds. Metabolic Effects of Alcohol. Clinics in Endocrinology and Metabolism, Vol. 7., No. 2, 1978. pp. 351-367.

Wright, S.G., and Ree, G.H. Blood in the alcohol stream (letter). Lancet 1:49, 1978.

Wynder, E.L. Toward the prevention of laryngeal cancer. Laryngoscope 85:1190-1196, 1975.

Wynder, E.L., and Chan, P.C. The possible role of riboflavin deficiency in epithelial neoplasia. II. Effect on skin tumor development. Cancer 26: 1221-1224, 1970.

Yadav, H.S.; Chaudhuri, B.N.; and Mukherjee, S.K. Effect of ethyl alcohol on thyroidal iodide trapping and renal clearance of ^{131}I label in rats. Indian Journal of Medical Research 58: 1421-1427, 1970.

Ylikahri, R.H.; Huttunen, M.O.; and Harkonen, M. Effect of alcohol on anterior-pituitary secretion of trophic hormones. Lancet 1:1353, 1976.

Ylikahri, R.; Huttunen, M.; Harkonen, M.; Seuderling, U.; Onikki, S.; Karonen, S.-L.; and Adlercreutz, H. Low plasma testosterone values in men during hangover. Journal of Steroid Biochemistry 5:655-658, 1974.

Young, G.P.; Dudley, F.J.; and Van-der-Weyden, M.B. Suppressive effect of alcoholic liver disease sera on lymphocyte transformation. Gut 20: 833-839, 1979.

Zeus, J. Histologische Untersuchungen und distalen Oesophagus zur Pathogenese der Oesophagitis unter besonderer Beruecksichtigung der Beziehung zum Sodbrennen [Histological research on the distal esophagus and pathogenesis of esophagitis, with special consideration of its relationship to heartburn]. Dissertation Erlangen. 1970.

Chapter V

The Effects of Alcohol on Pregnancy Outcome

Clinical reports and experimental studies published in the past 10 years leave little doubt that prenatal alcohol exposure poses a threat to the health of the unborn child. This threat ranges from miscarriage and newborn death, to a cluster of abnormalities called fetal alcohol syndrome (FAS), to subtle behavioral disturbances such as hyperactivity, which may occur in the absence of observable physical abnormalities.

This chapter represents a selective review and status report on current knowledge concerning the effects of alcohol on pregnancy outcome. It is not intended to be exhaustive. A number of recent more detailed reviews have dealt with a full range of issues involving alcohol-related pregnancy complications and birth defects (see, for example, Rosett and Weiner 1981; Rosett et al. 1981; Sokol 1981, 1982; Abel 1982a; Randall 1982). In addition, overviews of fetal alcohol research are contained in the Third and Fourth Special Reports to the U.S. Congress on Alcohol and Health (USDHEW 1978; USDHHS 1981).

The present survey examines current findings about alcohol and pregnancy and needs for future research. The first section begins with a brief historical introduction. This is followed by an examination of data documenting alcohol as a teratogen (a substance that can cause birth defects). Some specific alcohol-related pregnancy complications and birth defects are then examined, with particular emphasis on new information about brain damage and behavioral disorders. The need for further information about time of exposure, patterns of drinking, type of beverage, determination of dose/response relations and thresholds, and host susceptibility are discussed in conjunction with ways of improving pregnancy outcomes by preventing alcohol-related birth defects.

It should be noted that this chapter uses, where appropriate, the terms alcohol-related birth effects as well as alcohol-related birth defects. Birth defects include entities such as organ anomalies. The term birth effects, as used in this chapter, is more inclusive and contains, in addition, pregnancy complications and outcomes such as small-for-gestation-age weight. These factors usually place the infant at higher risk for an adverse health occurrence, but are not in their own right anomalies.

Historical Perspective

Although even during ancient times alcohol may have been considered a pregnancy risk, by the 1700s a link between alcohol and birth defects was strongly suspected. In 1759, for example, the London College of Physicians petitioned the British Parliament to reinstate taxes on gin so that it would be less available and, therefore, would constitute less of a risk to pregnant women and their infants (Warner and Rosett 1975). Despite reinstatement of these taxes, a steady outpouring of warnings about drinking during pregnancy continued, indicating that the problem did not disappear after the law was changed.

In 1899, a report appeared in England which documented in a novel way many of the adverse effects of alcohol during pregnancy (Sullivan 1899). Six hundred offspring of 120 alcoholic women in a Liverpool jail were compared with offspring born to 28 nondrinking female relatives of these women. Infant mortality and stillbirth rates for the alcoholics' children were 2-1/2 times higher than the rates among offspring of the comparison group. Even more dramatic was the finding that many of those alcoholic women who previously had infants with severe and often fatal complications gave birth to healthy children when forced to become abstinent because of imprisonment. The obvious inference drawn by the author was that alcohol is toxic to the fetus.

Although several relevant studies pointing to fetal damage from prenatal alcohol exposure were performed during the early 20th

century, interest in alcohol and pregnancy notably decreased during Prohibition, and only sporadic reports can be found in the world literature from the succeeding 50 years (Sokol 1982; Abel in press). Modern recognition awaited the publication of two key papers in 1973 by Jones, Smith, and their colleagues. These investigators reported that 11 children of chronically alcoholic mothers were growth-retarded and had craniofacial and cardiac defects, as well as developmental delay (Jones and Smith 1973; Jones et al. 1973). Perhaps, in retrospect, the major contribution of these papers was the coining of the term fetal alcohol syndrome, which refocused interest on important scientific and public policy questions. These reports gave particular impetus because they appeared during a period of increased public and professional concern with maternal/fetal/infant health. If alcohol consumption represented an important and potentially avoidable pregnancy risk, perhaps pregnancy outcomes could be improved when the risk had been recognized.

Fetal Alcohol Syndrome and Alcohol-Related Birth Effects

Numerous cases of fetal alcohol syndrome from all over the world have now been described in the scientific literature, e.g., from Australia, Belgium, Brazil, Canada, Chile, Czechoslovakia, France, Germany, Hungary, Ireland, Italy, Japan, South Africa, Spain, Sweden, Switzerland, and the United States (Abel in press). Because standardized criteria were not used for many of the diagnoses, the Fetal Alcohol Study Group of the Research Society on Alcoholism proposed specific criteria in 1980 (Rosett 1980). These criteria require that at least one feature from each of the following three categories be present for a diagnosis of fetal alcohol syndrome:

- Growth retardation before and/or after birth
- A pattern of abnormal features of the face and head, including small head circumference, small eyes, or evidence of retarded formation of the midfacial area, including a flattened bridge and short length of the nose, and flattening of the vertical groove between the nose and mouth, i.e., the philtrum
- Evidence of central nervous system abnormality, including, for example, abnormal neonatal behavior, mental retardation, or other evidence of abnormal neurobehavioral development

None of these features alone is specifically characteristic of fetal exposure to alcohol. In fact, many other nonspecific abnormalities are seen in conjunction with FAS, as well as in isolation, which makes diagnosis difficult. These include eye and ear defects; heart murmurs, which are often associated with septal defects (openings between the chambers of the heart); genitourinary anomalies, such as undescended testicles; hemangiomas (a type of birthmark); fingerprint and palmar crease abnormalities; and other anomalies, such as hernias. Any of these abnormalities may be seen individually, even without maternal drinking. However, when these conditions are seen in conjunction with a pattern of abnormalities consistent with FAS, the diagnosis of FAS may be made. Alcohol-related birth effects are complications of pregnancy, risk associated pregnancy outcomes (e.g., small-for-gestation-age weight), and birth defects that can be attributed to alcohol use after statistical analysis has corrected for the contribution of other possible factors.

Prevalence

The reported prevalence of FAS varies widely and no firm national data are as yet available. Depending on the location and the population under study, the overall prevalence has varied from 0.4 per 1,000 in Cleveland (Sokol et al. 1980) to 2.1 per 1,000 in Boston (Rosett et al. 1983). In Seattle, where the syndrome was first identified, one study indicated a prevalence of 1.3 per 1,000 (Hanson et al. 1978). Estimates from Europe have ranged from 1.6 per 1,000 in Sweden (Olegard et al. 1979) to 2.9 per 1,000 in France (Dehaene et al. 1977). It appears then that, calculated on the basis of total number of births, the overall prevalence of FAS is in the range of 1 to 3 per 1,000.

Estimates of the frequency of the full fetal alcohol syndrome, calculated on the basis of occurrence only among women who have been identified as problem drinkers or alcohol abusers, are somewhat more consistent and higher than the above figures, ranging from 23 to 29 per 1,000 (Hanson et al. 1978; Sokol et al. 1980; Rosett et al. 1983). Further, as might

be expected, alcohol-related birth effects have been reported considerably more frequently among alcohol abusers. However, the estimates vary widely, ranging from 78 per 1,000 to 690 per 1,000 (Ouellette et al. 1977; Hanson et al. 1978; Sokol et al. 1980). This wide range may be attributed to the differing criteria used for inclusion in this diagnostic category. Thus, although only a limited proportion of the offspring may have enough abnormalities to be diagnosed as FAS, some effects possibly attributable to alcohol appear to occur in relatively high proportions of infants born to women who drink heavily during pregnancy.

In general, about 65 to 70 percent of developmental defects have been noted to be of unknown origin (Wilson 1973). Sokol (1981) has calculated that about 5 percent of all congenital anomalies may be attributable to prenatal alcohol exposure, suggesting that alcohol may account for a significant proportion of previously unexplained anomalies and that it should be considered a major contributor to abnormal fetal development. In terms of mental retardation, which may be considered the most serious and damaging of all alcohol-related birth defects, Clarren and Smith (1978) have stated that maternal alcohol abuse during pregnancy "appears to be the most frequent known teratogenic cause of mental retardation in the Western World."

The high prevalence of alcohol-related birth defects is worth noting not only because of its impact on the affected individual and on society, but also because of its significant economic impact. While difficult to evaluate precisely, one study has estimated a lifetime cost of $155 million for those born in a given year with FAS and alcohol-related birth defects in New York State alone (Russell 1980).

Problems with Human Fetal Alcohol Studies

The experimental administration of alcohol to pregnant women is clearly unethical. Studies of alcohol and pregnancy in humans are limited by virtue of the usual constraints associated with human subjects to clinical observation and nonmanipulative designs. Clinical reports have been of particular importance in special cases, such as in the birth of twins. For example, a case in which one fraternal twin was more severely affected with FAS than the other (Christoffel and Salafsky 1975) suggests that genetic factors are significant in determining fetal susceptibility to alcohol's damaging effects. This may partially explain why only one of two women who consume the same amount of alcohol may give birth to a child with FAS.

Observational studies involving many patients rather than single cases, however, can be more difficult to interpret. Recent detailed critical reviews of such studies (Neugut 1981; Sokol 1980b) have identified two general problem areas, the first involving the issue of bias. In many published case reports and studies, the clinician diagnosing alcohol-related birth defects may have been aware of maternal alcohol abuse, leading to the possibility that some of the observed associations may have been affected by such knowledge. However, even when infants have been examined without knowledge of maternal alcohol history, as in the large prospective observational studies funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), alcohol-related pregnancy complications and birth effects, including lowered birth weight and congenital abnormalities, have been identified (Ouellette et al. 1977; Kuzma and Sokol 1982).

A second major problem in human fetal alcohol studies is called "confounding." Alcohol is but one of a multitude of possible pregnancy risks (cofactors) which include maternal characteristics, medical disorders, pregnancy complications, abuse of substances other than alcohol, and exposure to environmental contaminants. In observational study designs, complex statistical techniques are used to try to control and adjust for as many factors as possible to support the inference that any observed effect is attributable to alcohol. Many pregnancy risks remain unknown, however, and these statistical techniques are limited, making it almost impossible to adjust for confounding completely. While human studies can document associations between alcohol and adverse pregnancy outcome, they cannot demonstrate causality convincingly (Sokol 1980b). Experimental studies in animals have therefore proven to be valuable. If rigorously designed and performed, animal studies allow greater control and greater certainty in inferring a causative role for alcohol as a teratogen.

Animal Models

Alcohol-related birth defects comparable to those occurring in humans have been reported among mice (Randall and Taylor 1979), rats

(Abel 1979), beagles (Ellis and Pick 1980), sheep (Potter et al. 1980), miniature swine (Dexter et al. 1980), and monkeys (Altshuler and Shippenberg 1981). These studies in animals have documented direct dose/response effects of alcohol on perinatal mortality, infant weight, and soft tissue malformation and have shown that these effects cannot be attributed to other factors, such as undernutrition, often associated with alcohol abuse in humans. For example, Randall and her colleagues (1981), using a study design that equates the nutritional intake of alcohol-exposed and control animals, clearly demonstrated in mice that restricted caloric intake could not account for the teratogenic effects observed. However, nutritional factors, e.g., low protein intake, can interact with alcohol exposure, leading to higher blood alcohol levels and more severe alcohol-related birth defects, as suggested by the work of Wiener and her colleagues (1981). These findings indicate that nutritional factors alone did not account for the observed deficits. The alcohol present in the body rather than nutritional factors is the teratogen.

Other compelling evidence for a direct effect of alcohol as a teratogen comes from in vitro (literally in glass) studies of embryonic tissue. In these experiments, rat embryos have been directly exposed to alcohol (Brown et al. 1979). Compared with unexposed controls, embryos exposed to 0.15 or 0.3 grams of alcohol per 100 ml of culture medium (an intoxicating dose) had decreased crown-rump and head lengths and decreased total cell counts, as well as retarded development, after only 24 hours of exposure. The rat embryo at this stage cannot metabolize alcohol to its primary metabolite, acetaldehyde; thus, this study strongly supports a causative role for alcohol as an agent directly toxic to the fetus but does not rule out the possibility that acetaldehyde also may be a teratogen (Popov et al. 1981).

Additional support for a direct effect of alcohol in inducing aberrant fetal development is provided by a notable study performed in mice. Sulik and her colleagues (1981) administered early in pregnancy two large closely spaced doses of alcohol on a single day, such as might occur in binge drinking. They were able to produce abnormal facial features in the mouse fetus that appear remarkably similar to those observed in human FAS. However, certain methodological issues raise questions as to the immediate applicability of such findings to humans. Nonetheless, this study both supports the concept of a causative role for alcohol in inducing fetal malformation and raises questions about the critical periods of exposure for specific effects and the ability of fetal tissues to recover from exposure to toxic levels of alcohol early in pregnancy.

Specific Adverse Pregnancy Outcomes

Exposure to intoxicating levels of alcohol over prolonged periods is clearly associated with a range of specific adverse fetal outcomes. Some of these outcomes have been described in detail in the Third and Fourth Special Reports to the U.S. Congress on Alcohol and Health (USDHEW 1978; USDHHS 1981) and therefore will be reviewed only briefly.

Spontaneous Abortion

The risk for spontaneous abortion (miscarriage or early pregnancy loss) is increased approximately twofold in pregnancies complicated by maternal drinking, although perhaps only among the heaviest or most frequent drinking 3 to 5 percent of women (Harlap and Shiono 1980; Kline et al. 1980; Sokol 1980a; Sokol et al. 1980). Pregnant monkeys also tend to abort early in pregnancy following alcohol exposure (Altshuler and Shippenberg 1981), as do rodents, as indicated by an increased rate of resorption, the analog of spontaneous abortion in humans (Chernoff 1977; Randall et al. 1981). With respect to later pregnancy loss, i.e., the stillbirth rate, the data are less clear. A statistically significant increase in the stillbirth rate was detected in an initial study from France for women consuming three or more drinks per day (Kaminski et al. 1978), but not in a subsequent study by this group (Kaminski et al. 1981). Also, no increase in the stillbirth rate was noted in a large study from the Cleveland area (Sokol et al. 1980). Studies in animals are likewise equivocal with respect to alcohol and stillbirths (Ellis and Pick 1980; Abel et al. 1981b).

Physical Congenital Anomalies

Virtually all of the congenital anomalies reported to be alcohol-related birth defects in humans have now been duplicated in animals prenatally exposed to alcohol, although probably only when blood alcohol levels exceeded 0.1 percent--the legal level of intoxication in most States (Randall 1982). Acute intragastric

administration (directly into the stomach) of alcohol to mice on one day of pregnancy did not result in a significant increase in birth defects, compared with two nutritional control groups (Lochry et al. 1982). Thus, it appears that duration as well as level of exposure are important determinants of alcohol-related physical birth defects.

Lowered Birth Weight

Lowered birth weight is the most reliably observed effect attributable to in utero alcohol exposure in humans and animals. Based on a review of more than 300 reported cases of FAS, the average birth weight of such children was 2,000 grams (Abel 1982b), compared with the median birth weight for all infants in the United States of more than 3,300 grams (NCHS 1980). Further, decreased birth weight has been observed even in the absence of full FAS (Ouellette et al. 1977; Sokol et al. 1980). These findings are of concern because lowered birth weight is widely recognized as being associated with significant increases in risk for fetal and infant mortality and long-term abnormalities in neurologic development and intelligence. Lowered birth weight may be the result of preterm delivery (prematurity) or intrauterine growth retardation, or both.

Preterm delivery.--Effects of alcohol on pregnancy duration are unclear. Alcohol-related prematurity was not identified in one study of more than 12,000 pregnancies (Sokol et al. 1980). Two more recent studies, however, suggest that preterm delivery may result from prenatal alcohol exposure. Berkowitz (1981), in a study of 175 mothers of preterm infants and 313 mothers of term infants, found that alcohol consumption prior to the third trimester of pregnancy was associated with preterm delivery. Furthermore, in a more detailed analysis of the same data, Berkowitz and her coworkers (1982) found that heavier alcohol consumption (an average of two or more drinks every day) during pregnancy was associated with an approximately threefold increase in risk for preterm delivery; no increased risk was identified for lighter drinking.

In a recent study from Boston City Hospital of 1,690 births, maternal drinking prior to pregnancy was found to be associated with shortened gestation (Hingson et al. 1982). It is interesting to note that preterm delivery does not occur in pregnant animals that are given alcohol--in fact, parturition may be delayed (Bond 1982).

Intrauterine growth retardation.--In contrast to the data involving prematurity, the evidence linking in utero alcohol exposure and decreased fetal growth is very strong. For example, in their study of more than 12,000 pregnancies, Sokol and his colleagues (1980) found that with alcohol abuse birth weight was decreased by about 190 grams, in the absence of any effect on pregnancy duration. Similarly, in another group of approximately 5,000 women in a different part of the country, Kuzma and Sokol (1982) detected about a 100-gram decrement in birth weight, limited to the most frequently drinking 3 percent of women. Little (1977) noted a statistically significant decrease in infant birth weight of 91 grams for women reporting average alcohol use of 1 ounce (two drinks) per day for the prepregnancy period, and a 160-gram decrement for late pregnancy consumption at that level.

Prenatal growth retardation associated with maternal alcohol consumption has been observed in numerous animal studies (Ellis and Pick 1980; Lee and Leichter 1980). The extent of this retardation appears to be dose-dependent with exposure during the third trimester having a more severe effect on birth weight than did exposure earlier in gestation (Abel 1979; Lochry et al. 1982). The decrease in birth weight can be seen even after a single administration of alcohol shortly before term (Greizerstein and Abel 1979; Lochry et al. 1982). These observations are consistent with studies in humans that indicate that drinking continued through the third trimester is associated with decreased infant weight (Little 1977; Rosett et al. 1978).

Studies in animals are also beginning to help identify mechanisms by which alcohol may decrease fetal growth. For example, animal embryos provide evidence for the direct effects of alcohol and acetaldehyde on fetal growth (Brown et al. 1979; Popov et al. 1981). In addition, alcohol exposure may lead to chronic fetal hypoxia (Abel 1982b), or to hypoglycemia, i.e., low blood glucose. Decreased fetal nutrition resulting from hypoglycemia induced by high blood alcohol levels could contribute to fetal growth retardation (Tanaka et al. 1982). Other studies suggest that alcohol may affect fetal cell growth by interfering with the passage of amino acids across the placenta (Henderson et al. 1981). With inadequate transport of amino acids to the fetus, protein synthesis and growth would be inhibited. Moreover, decreased incorporation of amino acids into protein in alcohol-exposed fetuses has also been reported (Henderson et

al. 1979, 1980). Although alcohol-related decreased absorption of zinc has also been suggested as a contributor to growth retardation, the evidence on this issue is contradictory (e.g., Samson and Diaz 1981; Flynn et al. 1981; Ghishan et al. 1982).

Based on these results, it is reasonable to conclude that alcohol is associated with lowered birth weight, related possibly to both shorter gestation and decreased intrauterine growth. Diminished prenatal growth is dose-related and may be more severe when alcohol is consumed in the third trimester.

Abnormal Neurobehavioral and Neural Development

In surviving fetuses, the most severe alcohol-related birth defects are those involving the central nervous system. Congenital anomalies, even those that are very severe, e.g., heart defects, are often repairable. Brain damage, however, is permanent and irreversible. Alcohol-related anatomical, electrophysiological, and biochemical abnormalities in the brain have now been identified and may underlie the observed behavioral deficits.

Behavioral development.--The adverse effects of alcohol on behavioral development may be divided into three main categories: abnormal neonatal behavior, as reflected in sleep problems and state regulation disorders; childhood hyperactivity; and mental retardation, as indicated by lowered IQ scores (Abel 1981a).

Infants born to heavy drinkers or alcoholics have been found to be more restless during sleep and not to sleep as much as other children (Rosett et al. 1979). Abnormal electroencephalographic (EEG) activity during sleep has been noted for as long as 6 weeks after birth in some of these children.

Hyperactivity in children with FAS has been noted in several clinical case studies (Abel 1981a). It has also been noted in 15 children who had physical abnormalities consistent with FAS, but whose IQ scores were within normal limits. All 15 of these children eventually received recommendation for special education services because of their restlessness, short attention spans, and distractibility (Shaywitz et al. 1980).

Lowered IQ scores in conjunction with heavy prenatal alcohol exposure have been noted in other countries. In the United States, the average IQ scores for a group of patients with FAS was found to be 63, reflecting moderate mental retardation (Streissguth et al. 1978a), and when the same individuals were retested, the IQ scores did not change (Streissguth et al. 1978b). Similar results were obtained in the study from Sweden in which children with physical signs of FAS were found to have an average IQ below 70 (Olegard et al. 1979).

Two studies of mental and motor development identified infants exposed in utero to alcohol and investigated those who did not exhibit full FAS. Streissguth and her coworkers (1980) administered an infant development test to a group of infants at the age of 8 months. They recorded significant trends toward lower scores on mental and motor tests related to increased maternal alcohol use during pregnancy.

Golden and her colleagues (1982) evaluated neurobehavioral development in 12 infants with physical alcohol-related birth defects and a history of maternal alcohol abuse and compared them with 12 normal infants. These two groups of infants were examined at a mean age of 1 year without knowledge of the prenatal drinking history. Both the mental and motor scores were 20 points lower in the alcohol group, a notable difference. Furthermore, the alcohol group had significantly higher frequencies of postnatal growth retardation and microcephaly, i.e., abnormally small heads. Although it was not possible in this study to adjust for the confounding effects of maternal smoking, there was strong evidence that the abnormal neurobehavioral development of the infants was attributable to alcohol alone or in combination with cigarette smoking.

Landesman-Dwyer and her coworkers (1981) studied 272 offspring of women without alcohol problems and found that at age 4, the children with greater in utero alcohol exposure generally were less attentive and less compliant with parental commands. More recently, Streissguth and her colleagues (1983b), after observing 4-year-olds, found that maternal alcohol use during pregnancy is significantly related to decreased attention and longer reaction time. They suggested that alcohol use by pregnant women can have long-term behavioral effects in children.

As with physical anomalies, some studies in animals duplicate many of the behavioral abnormalities noted in humans with fetal alcohol exposure. For example, hyperactivity has been noted consistently in rats prenatally exposed to alcohol (Bond and DiGiusto 1976; Abel 1982c). Learning difficulties have also been identified in animals prenatally exposed to

alcohol (Bond and DiGiusto 1978; Riley et al. 1979a, b; Abel 1979). Riley and his coworkers (1979a, b) have proposed that many of the abnormal behavioral effects related to prenatal alcohol exposure suggest an underlying problem in response inhibition. The magnitude of this effect appears to be dose-related (Lochry and Riley 1980). On balance, the behavioral abnormalities found in animals are similar to those in children with fetal alcohol syndrome.

Neural development.--Neuroanatomic and biochemical abnormalities probably underlie alcohol-related abnormal neurobehavioral development; these areas are currently under study. Microcephaly, an important component in the diagnosis of FAS, indicates an overall decrease in brain growth. Moreover, anatomic abnormalities have been observed in brains of children born to alcoholic women as studied at autopsy, as well as in animals prenatally exposed to alcohol. These include hydrocephalus (increased fluid distending cavities in the brain), absence of the corpus collosum (the bundle of fibers connecting the two sides of the brain), and abnormal growth patterns of nerve and other brain cells (Clarren et al. 1978; Peiffer et al. 1979; Rasmussen and Christensen 1980).

Subtle changes in brain structure have been noted in animals following prenatal alcohol exposure. West et al. (1981) found that rats exposed to alcohol throughout gestation had abnormally distributed nerve fibers in the hippocampus (deep inside the brain), and Barnes and Walker (1981) identified a decrease in the cell content of rats' hippocampus. In addition, Davies and Smith (1981) identified a considerable decrease in the extent of the neural dendrites (parts of the nerve cell that receive signals) of the hippocampus in mice. Taken together, these anatomic abnormalities in the hippocampus may be the structural basis for some of the behavioral abnormalities observed in humans and animals, as this part of the brain is involved in learning/memory performance and in inhibitory control of behavior.

Alcohol Use, Abuse, and Dependence and Pregnancy

Drinking in Women

Approximately 60 percent of adult American women drink alcoholic beverages; 40 percent are abstinent. An estimated 6 percent of adult women in this country have been classified as problem drinkers (Clark and Midanik 1982). During the peak reproductive age range of 18-34, an estimated 5 percent of American women consume an average of 2 or more drinks per day or 14 or more drinks per week (Clark and Midanik 1982). Estimates of the proportion of women who drink at least this amount during pregnancy vary widely, ranging from a low of 0.5 percent in parts of California (Harlap and Shiono 1980) to a high of 16 percent in Buffalo (Russell and Bigler 1979), and a median of 2 percent (Abel in press). Because alcohol readily crosses the placenta, yielding levels of alcohol in the fetus almost identical to those in the mother, it is reasonable to conclude that a significant number of unborn children in the United States are exposed to the equivalent of two drinks a day.

Drinking Patterns in Pregnancy

The amount and timing of alcohol consumption that put the fetus at risk are still unknown. Scientists have considerable difficulty in addressing this issue because of problems in obtaining reliable drinking histories and in defining abusive drinking and dependence. Furthermore, drinking patterns often change during pregnancy.

Essentially all reported studies of drinking during pregnancy have relied on self-reports of patients. The inherent limitations of self-reports suggest that the alcohol intake information obtained must be understood in broad terms, rather than in precise measurements. The amount of alcohol actually imbibed in a drink might vary from 1 to 8 ounces, depending on the individual giving the history and the method by which the history is obtained (Rosett et al. 1983). A detailed recall of drinking behavior is likely to be inexact, particularly for the heavy or dependent drinker who may be unable or unwilling to recall specifically how much she drank. Self-reports of drinking during pregnancy are therefore of limited value. This in turn seriously limits the credibility of estimates relating a given number of drinks per day to a particular risk to the fetus. Moreover, it is likely that actual alcohol intake is underreported by the abusive drinker, the individual most likely to be at risk for giving birth to a child with alcohol-related birth defects (Sokol et al. 1981). This could lead investigators to overestimate the risk to the fetus of what might appear to be "two drinks a day."

All investigators studying drinking during pregnancy have been faced with the problems

of obtaining reliable drinking histories and have used a multitude of definitions of problem drinking, abusive drinking, heavy drinking, and alcohol dependence. For example, studies by Rosett et al. (1981), Streissguth et al. (1981), and Kuzma and Kissinger (1981) all used different criteria. Such variances in definition increase the difficulty of making comparisons across studies.

The stage of pregnancy is an important consideration in assessing women's drinking habits because women tend to decrease the amount they drink as pregnancy progresses, an observation first reported by Little et al. (1976) and subsequently corroborated by others (e.g., Rosett et al. 1978; Sokol et al. 1981; Weiner et al. 1983) and by the National Center for Health Statistics neonatality survey as discussed in chapter 1 of this report. Fried and his coworkers (1980) in a study of 217 Canadian women found that prior to pregnancy 18 percent of women were heavy (0.85 ounces per day) social drinkers, but that during the first trimester this proportion was reduced by two-thirds. The proportion of women who were drinking heavily continued to decrease during the last two trimesters of pregnancy. In the Cleveland study (Sokol et al. 1981), the heavier drinking group also was found to decrease its alcohol intake significantly as gestation progressed. These are encouraging findings, inasmuch as decreases in drinking would be expected to minimize birth defects. They point up the problem, however, of attempting to summarize a woman's drinking throughout pregnancy with a single number, e.g., "two drinks a day."

Paternal Drinking

Women who drink heavily tend to be married to men who drink heavily (Gomberg 1975). This suggests that some of the abnormalities described as alcohol-related birth defects might be related to paternal drinking. Long-term consumption by men of large amounts of alcohol is known to be associated with impotence, reduced sperm motility and ultimately loss of sperm, and abnormalities in sperm structure (Lester and Van Thiel 1977). Thus, fertilization with defective sperm is possible, which might result in fetal anomalies. Some investigators have argued that the male parent could contribute to alcohol-related birth defects (Anderson et al. 1981); however, no convincing evidence exists of such paternally mediated anomalies related to alcohol. Recently, Kuzma and Sokol (1982) examined 44 potential determinants of infant birth weight adjusted for gestational age and found no significant effect of paternal alcohol consumption. Similarly, Randall and her coworkers (1982) were unable to detect any effects of chronic paternal alcohol consumption on fetal growth and development in mice, in terms of the number of implantation sites, prenatal mortality, fetal weight, sex ratio, or the frequency of soft tissue malformation. These findings were confirmed by Bennett et al. (1982). Some studies reporting paternally mediated alcohol effects in conjunction with alcohol have had such methodologic flaws as lack of nutritional controls.

Knowledge and Attitudes

Public education efforts concerning risks associated with alcohol use during pregnancy have been actively pursued since the mid-1970s. Broad coverage in the media has been obtained for public health advisories from NIAAA, the American Medical Association, and the March of Dimes on a national level, as well as for an advisory from the Surgeon General (FDA 1981). Public education has also been attempted by many State governments. Most Americans have been exposed to such public health messages, and 90 percent of the respondents in a recent survey knew that drinking during pregnancy might be harmful. However, three-quarters of the respondents who thought abstinence is unnecessary believed that an average of more than three drinks per day was safe (Little et al. 1981). These findings suggest that current public education/prevention programs may not be fully adequate in permeating the public consciousness.

Although knowledge of potential adverse effects of alcohol on pregnancy outcome has changed, and public attitudes have shifted over the past 10 years, the question remains: Has the drinking behavior of women during pregnancy changed? The purpose of a recent study was to compare drinking patterns during pregnancy in the same population in Seattle over a 6-year interval (Streissguth et al. 1983a). Samples of pregnant women were interviewed in 1974-75 and in 1980-81. Although the proportion of women drinking during pregnancy was found to have decreased during the 6-year interval, the proportion of women drinking at least an ounce of absolute alcohol (two drinks) each day was relatively constant. Because precisely this limited proportion of the population incurs the highest risk for al-

cohol-related birth defects, these findings suggest cause for concern.

Conclusions

Although studies of drinking during pregnancy depend upon self-report and the reliability and precision of such data are limited, it appears that drinking during pregnancy is not uncommon. Many women who drink either decrease their drinking naturally or become abstinent during pregnancy. Public education efforts may well reinforce this change in behavior. However, persistently heavy drinking during pregnancy remains a problem for some women despite public education efforts.

Implications of Current Knowledge—Frontiers

The preceding sections have summarized the current status of information concerning risks for alcohol-related dangers to pregnancy and birth defects. Progress in scientific evaluation of these risks has clearly been very rapid over the past decade. However, it is equally clear that many questions remain.

Need for Further Research

Timing, pattern, and beverage source.-- Because a reliable biochemical indicator for alcohol intake is not available, clinical investigators must depend on patient reports. However, as previously noted, human drinking is difficult to represent numerically in a single (and simple) measure of alcohol use; volume, frequency, and beverage source of alcohol intake must be considered. Also, other potential determinants of pregnancy outcome, e.g., other substance use, medical/obstetric factors, and socioeconomic status should be taken into account.

Improved measures of alcohol intake would heighten understanding of the stages of pregnancy when drinking is most dangerous to the fetus. Different alcohol-related birth defects might result from drinking during different critical periods, e.g., either early or late in pregnancy. Sulik and her colleagues (1981) suggest that heavy alcohol consumption early in pregnancy might contribute to such birth defects as abnormalities in the face and central nervous system. Studies of the relationship between early pregnancy drinking, particularly binge drinking, and physical congenital anomalies in the human could be valuable.

Heavy drinking in late pregnancy leads to an increased frequency of congenital anomalies (Rosett et al. 1978; Rosett and Weiner 1981). Although organogenesis, the development of the organs of the embryo, may be completed during very early pregnancy, nerve cells, for example, continue to make new connections through pregnancy. Heavy drinking could impair the growth of these connections. The results of animal studies suggest that after toxic substances are withdrawn, the fetus may compensate for earlier impairments with accelerated growth and repair before development is completed (Snow and Tam 1979; Anders and Persaud 1980). Further basic science studies in animals and clinical research in humans regarding critical periods of exposure and the capacity of the unborn offspring for compensatory growth and repair are needed, because the results of such studies might be useful in counseling patients whose fetuses have been exposed to significant levels of alcohol during early pregnancy.

Beverage source (wine, beer, whisky, etc.) may affect infants differentially. Animal studies have been few and inconclusive (Abel 1981b; Abel et al. 1981b). Nonetheless, possible relationships between beverage source and pregnancy outcome have been reported (Kaminski et al. 1978; Kuzma and Sokol 1982; Berkowitz et al. 1982).

Moderate drinking.--Moderate drinking may increase the risk for lowered birth weight (Little 1977), abnormal neurobehavioral development (Streissguth et al. 1980), and spontaneous abortion (Harlap and Shiono 1980; Kline et al. 1980). However, others (Rosett 1980; Sokol 1980b, 1982) have questioned whether the women manifesting these increased pregnancy risks are in fact moderate drinkers. They note that the women with alcohol-related pregnancy risk constitute only the heaviest drinking (5 to 10 percent) of pregnant women. As research continues to expand knowledge, the answers to this important clinical question will emerge.

Susceptibility.--Different species and different strains within a species of animal may differ in their susceptibility to alcohol-related birth defects. Also, differences among animals in the same exposed litter are commonly observed. As noted earlier, human fraternal twins may not be equally affected by alcohol exposure (Christoffel and Salafsky 1975). Such findings suggest the possibility of differential susceptibility on a genetic basis. Interactions

of alcohol consumption with other pregnancy risks, such as poor nutrition, other substance use, or medical illnesses, may also alter susceptibility. Information about interacting risks would help in designing more focused and potentially more effective prevention strategies. A profile of patients particularly at risk for the adverse effects of in utero alcohol exposure also would aid the practitioner in giving direct patient care.

Prevention and Treatment

Problems.--Although major progress has been made over the past decade in understanding the risks of alcohol use during pregnancy, much remains unknown. Methods are being developed to identify and treat pregnant women with alcohol problems (Rosett et al. 1981; Sokol et al. 1981). Education programs aimed at professionals may modify attitudes and clinical behavior (Weiner et al. 1982; Little et al. 1983). Professional education, based on firm scientific evidence concerning risks for alcohol-related birth defects, effective methods of detection of abusive drinking, and treatment methods for abusive drinking and alcohol dependence, appears to be a promising avenue for the prevention of alcohol-related birth defects and other anomalies.

Current statements and recommendations.--Based on currently available information, some broad statements with prevention and treatment implications appear to be warranted. Extensive public education efforts have alerted women to the dangers and fewer American women appear to be drinking during pregnancy. However, the frequency of heavy or abusive drinking may not have decreased. It can be stated with some certainty that those pregnant women who are the heaviest (most frequent) drinkers (about 5-10 percent) are exposing their unborn children to a significant risk. If these women abstain or significantly decrease their drinking during pregnancy, the evidence from both animal and human studies suggests that they can have healthier babies.

Effective prevention strategies for alcohol-related birth defects, including FAS, remain elusive. More information is needed about alcohol abuse and dependence in young women, so that more focused approaches to prevention can be developed. Professional education of physicians, nurses, and other health care providers may afford a rational and cost-effective approach to prevention of alcohol-related birth defects. If these individuals can be educated to take an active role in influencing the drinking habits of their patients, it may be possible to decrease the occurrence of alcohol-related birth defects and improve the probability of successful pregnancies.

Summary

Heavy drinking during pregnancy adversely affects organic and behavioral fetal development and increases the risks of miscarriage. When consumed in large amounts, alcohol can result in fetal alcohol syndrome. It appears that the overall prevalence of FAS is in the range of 1 to 3 cases per 1,000 births. Alcohol-related birth defects occur more frequently than FAS.

Alcohol can induce abnormal fetal development that varies in intensity, depending on dose, genetic susceptibility, nutritional status, and other as yet unknown factors. Heavy maternal drinking may affect the fetal nervous system, which may result in abnormal neonatal behavior, childhood hyperactivity, and mental retardation.

Alcohol probably affects all organ systems of the fetus, but many questions remain as to the mechanisms and their potential reversibility. Many variables, such as the amount of alcohol and the time during pregnancy of consumption, may influence the nature and degree of adverse effects. Studies in animals suggest that, at high alcohol levels, birth anomalies are directly related to the amount of alcohol exposure.

Public education efforts concerning risks associated with alcohol use have been actively pursued over recent years. These education efforts have encompassed media messages, public health advisories, and programs at the State level. Most Americans have been exposed to public health messages; however, the impact on heavier drinking in pregnancy has been less than desired. One study found that while the proportion of women who drank during pregnancy decreased over the past 6 years, the proportion of women drinking at least two drinks a day had not changed.

References

Abel, E.L. Prenatal effects of alcohol on adult learning in rats. Pharmacology, Biochemistry and Behavior 10:239-243, 1979.

Abel, E.L. Behavioral teratology of alcohol. Psychological Bulletin 90:564-581, 1981a.

Abel, E.L. Prenatal effects of beverage alcohol on fetal growth. Progress in Biochemical Pharmacology 18:111-114, 1981b.

Abel, E.L. Alcohol and Reproduction: A Bibliography. Westport, Conn.: Greenwood Press, 1982a.

Abel, E.L. Consumption of alcohol during pregnancy: A review of effects on growth and development of offspring. Human Biology 54:421-453, 1982b.

Abel, E.L. In utero alcohol exposure and developmental delay of response inhibition. Alcoholism: Clinical and Experimental Research 6:369-376, 1982c.

Abel, E.L. Marijuana, Tobacco and Alcohol Effects in Reproduction. Boca Raton, Fla.: CRC Press, in press.

Abel, E.L.; Dintcheff, B.A.; and Bush, R. Behavioral teratology of alcoholic beverages compared to ethanol. Neurobehavioral Toxicology and Teratology 3:339-342, 1981a.

Abel, E.L.; Dintcheff, B.A.; and Bush, R. Effects of beer, wine, whiskey and ethanol on pregnant rats and their offspring. Teratology 23:217-222, 1981b.

Altshuler, H.L., and Shippenberg, T.S. A subhuman primate model for fetal alcohol syndrome research. Neurobehavioral Toxicology and Teratology 3:121-126, 1981.

Anders, K., and Persaud, T.V.N. Compensatory embryonic development in the rat following maternal treatment with ethanol. Anatomischer Anzeigen 148:375-383, 1980.

Anderson, R.A.; Furby, J.E.; Oswald, C.; and Zaneveld, L.J.D. Teratological evaluation of mouse fetuses after paternal alcohol ingestion. Neurobehavioral Toxicology and Teratology 3: 117-120, 1981.

Barnes, D.E., and Walker, D.W. Prenatal ethanol exposure permanently reduces the number of pyramidal neurons in rat hippocampus. Developmental Brain Research 1:333-340, 1981.

Bennett, A.L.; Sorette, M.P.; and Greenwood, M.R.C. Effect of chronic paternal ethanol consumption on 19-day rat fetuses. Federation Proceedings 41:710, 1982.

Berkowitz, G.S. An epidemiologic study of preterm delivery. American Journal of Epidemiology 113: 81-92, 1981.

Berkowitz, G.S.; Holford, T.R.; and Berkowitz, R.L. Effects of cigarette smoking, alcohol, coffee and tea consumption on preterm delivery. Early Human Development 7:239- 250, 1982.

Bond, N.W. Prenatal exposure to ethanol: Association between increased gestational length and offspring mortality. Neurobehavioral Toxicology and Teratology 4:501-503, 1982.

Bond, N.W., and DiGiusto, E.L. Effects of prenatal alcohol consumption on open-field behaviour and alcohol preference in rats. Psychopharmacology (Berlin) 46:163-165, 1976.

Bond, N.W., and DiGiusto, E.L. Avoidance conditioning and Hebb-Williams maze performance in rats treated prenatally with alcohol. Psychopharmacology (Berlin) 58:69-71, 1978.

Brown, N.A.; Goulding, E.H.; and Fabro, S. Ethanol embryotoxicity: Direct effects on mammalian embryos in vitro. Science 206: 573-575, 1979.

Cahalan, D.; Cisin, I.H.; and Crossley, H.M. American Drinking Practices: A National Study of Drinking Behavio. and Attitude. Monograph No. 6. New Brunswick, N.J.: Rutgers Center of Alcohol Studies, 1969.

Chernoff, G.F. The fetal alcohol syndrome in mice: An animal model. Teratology 15:223- 229, 1977.

Christoffel, K.K., and Salafsky, L. Fetal alcohol syndrome in dizygotic twins. Journal of Pediatrics 87:963-967, 1975.

Clark, W., and Midanik, L. Alcohol use and alcohol problems among U.S. adults. Results of the 1979 national survey. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM)82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 3-52.

Clarren, S.K., and Smith, D.W. The fetal alcohol syndrome: A review of the world literature. New England Journal of Medicine 298:1063-1067, 1978.

Clarren, S.K.; Alvord, E.C.; Sumi, S.M.; Streissguth, A.P.; and Smith, D.W. Brain malformations related to prenatal exposure to ethanol. Journal of Pediatrics 92:64-67, 1978.

Davies, D.L., and Smith, D.E. Effects of perinatally administered ethanol on hippocampal development (abstract). Alcoholism: Clinical and Experimental Research 5:147, 1981.

Dehaene, P.; Samaille-Villette, C.; Samaille, P.; Crepin, G.; Walbaum, R.; Deroubaix, P.; and Blanc-Garin, A.P. Le syndrome d'alcoolisme foetal dans le nord de la France. [The fetal alcohol syndrome in the north of France.] Revue de l'Alcoolisme (Paris) 23: 145-158, 1977.

Dexter, J.D.; Tumbleson, M.E.; Decker, J.D.; and Middleton, C.C. Fetal alcohol syndrome in Sinclair (S-1) miniature swine. Alcoholism: Clinical and Experimental Research 4:146-151, 1980.

Ellis, F.W., and Pick, J.R. An animal model of the fetal alcohol syndrome in beagles. Alcoholism: Clinical and Experimental Research 4:123-134, 1980.

Flynn, A.; Miller, S.I.; Martier, S.S.; Golden, N.L.; Sokol, R.J.; and Del Villano, B.C. Zinc status of pregnant alcoholic women: A determinant of fetal outcome. Lancet 1:572- 575, 1981.

Food and Drug Administration. Surgeon General's Advisory on Alcohol and Pregnancy. FDA Drug Bulletin 11:9-10, 1981.

Fried, P.A.; Watkinson, B.; Grant, A.; and Knights, R.M. Changing patterns of soft drug use prior to and during pregnancy: A prospective study. Drug and Alcohol Dependence 6:323-343, 1980.

Ghishan, F.K.; Patwardhan, R.; and Green, H.L. Fetal alcohol syndrome: Inhibition of placental zinc transport as a potential mechanism for fetal growth retardation in the rat. Journal of Laboratory and Clinical Medicine 100:45-52, 1982.

Golden, N.L.; Sokol, R.J.; Kuhnert, B.R.; and Bottoms, S.F. Maternal alcohol use and infant development. Pediatrics 70: 931-934, 1982.

Gomberg, E.S. Alcoholism and Women: State of Knowledge Today. New York: National Council on Alcoholism, 1975. 12 pp.

Greizerstein, H.B., and Abel, E.L. Acute effects of ethanol on fetal body composition and electrolyte content in the rat. Bulletin of the Psychonomic Society 14:355-356, 1979.

Hanson, J.W.; Streissguth, A.P.; and Smith, D.W. The effects of moderate alcohol consumption during pregnancy on fetal growth and morphogenesis. Journal of Pediatrics 92:457-460, 1978.

Harlap, S., and Shiono, P.H. Alcohol, smoking and incidence of spontaneous abortions in the first and second trimester. Lancet 2:173-176, 1980.

Henderson, G.I.; Hoyumpa, A.M., Jr.; McClain, C.; and Schenker, S. The effects of chronic and acute alcohol administration on fetal development in the rat. Alcoholism: Clinical and Experimental Research 3:99-106, 1979.

Henderson, G.I.; Hoyumpa, A.M., Jr.; Rothschild, M.A.; and Schenker, S. Effect of ethanol and ethanol-induced hypothermia on protein synthesis in pregnant and fetal rats. Alcoholism: Clinical and Experimental Research 4:165-177, 1980.

Henderson, G.I.; Turner, D.; Patwardhan, R.V.; Lumeng, L.; Hoyumpa, A.M.; and Schenker, S. Inhibition of placental valine uptake after acute and chronic maternal ethanol consumption. Journal of Pharmacology and Experimental Therapeutics 216:465-472, 1981.

Hingson, R.; Alpert, J.J.; Day, N.; Dooling, E.; Kayne, H.; Morelock, S.; Oppenheimer, E.; and Zuckerman, B. Effects of maternal drinking and marijuana use on fetal growth and development. Pediatrics 70:539-546, 1982.

Jones, K.L., and Smith, D.W. Recognition of the fetal alcohol syndrome in early infancy. Lancet 2:999-1001, 1973.

Jones, K.L; Smith, D.W.; Ulleland, C.N.; and Streissguth, A.P. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 1:1267-1271, 1973.

Kaminski, M.; Rumeau-Rouquette, C.; and Schwartz, D. Alcohol consumption in pregnant women and the outcome of pregnancy. Alcoholism: Clinical and Experimental Research 2:155-163, 1978.

Kaminski, M.; Franc, M.; Lebouvier, M.; du Mazaubrun, C.; and Rumeau-Rouquette, C. Moderate alcohol use and pregnancy outcome. Neurobehavioral Toxicology and Teratology 3:173-181, 1981.

Kline, J.; Shrout, P.; Stein, Z.; Susser, M.; and Warburton, D. Drinking during pregnancy and spontaneous abortion. Lancet 2:176-180, 1980.

Kuzma, J.W., and Kissinger, D.G. Patterns of alcohol and cigarette use in pregnancy. Neurobehavioral Toxicology and Teratology 3:211-221, 1981.

Kuzma, J.W., and Sokol, R.J. Maternal drinking behavior and decreased intrauterine growth. Alcoholism: Clinical and Experimental Research 6:396-402, 1982.

Landesman-Dwyer, S.; Ragozin, A.S.; and Little, R.E. Behavioral correlates of prenatal alcohol exposure: A four-year followup study. Neurobehavioral Toxicology and Teratology 3:187-193, 1981.

Lee, M., and Leichter, J. Effect of litter size on the physical growth and maturation of the offspring of rats given alcohol during gestation. Growth 44:327-335, 1980.

Lester, R., and Van Thiel, D.H. Gonadal function in chronic alcoholic men. In: Gross, M. M., ed. Alcohol intoxication and Withdrawal. IIIa. Biological Aspects of Ethanol. Advances in Experimental Medicine and Biology 85a:399-414, 1977.

Little, R.E. Moderate alcohol use during pregnancy and decreased infant birth weight. American Journal of Public Health 67:1154-1156, 1977.

Little, R.E.; Schultz, F.A.; and Mandell, W. Drinking during pregnancy. Journal of Studies on Alcohol 37:375-379, 1976.

Little, R.E.; Grathwohl, H.L.; Streissguth, A.P.; and McIntyre, C. Public awareness and knowledge about the risks of drinking during pregnancy in Multnomah County, Oregon. American Journal of Public Health 71:312- 314, 1981.

Little, R.E.; Streissguth, A.P.; Guzinski, G.M.; Frathwohl, H.L.; Blumhagen, J.M.; and McIntyre, C.E. Change in obstetrician advice following a two-year community educational program on alcohol use and pregnancy. American Journal of Obstetrics and Gynecology 146:23-28, 1983.

Lochry, E.A., and Riley, E.P. Retention of passive avoidance and T-maze escape in rats exposed to alcohol prenatally. Neurobehavioral Toxicology and Teratology 2: 107-115, 1980.

Lochry, E.A.; Randall, C.L.; Goldsmith, A.A.; and Sutker, P.B. Effects of acute alcohol exposure during selected days of gestation in C3H mice. Neurobehavioral Toxicology and Teratology 4: 15-19, 1982.

National Center for Health Statistics. Monthly Vital Statistics Report: Annual Summary for the United States, 1979. Hyattsville, Md.: the Center, 1980.

Neugut, R.H. Epidemiological appraisal of the literature on the fetal alcohol syndrome in humans. Early Human Development 5:411-429, 1981.

Olegard, R.; Sabel, K.-G.; Aronsson, M.; Sandin, B.; Johansson, P.R.; Carlsson, C.; Kyllerman, M.; Iversen, K.; and Hrbek, A. Effects on the child of alcohol abuse during pregnancy: Retrospective and prospective studies. Acta Paediatrica Scandinavica (Supplement No. 275):112-121, 1979.

Ouellette, E.M.; Rosett, H.L.; Rosman, N.P.; and Weiner, L. Adverse effects on offspring of maternal alcohol abuse during pregnancy. New England Journal of Medicine 297:528-530, 1977.

Peiffer, J.; Majewski, F.; Fischbach, H.; Bierich, J.R.; and Volk, B. Alcohol embryo- and fetopathy: Neuropathology of three children and three fetuses. Journal of Neurological Science 41:125-137, 1979.

Popov, V.B.; Vaisman, B.L.; Puchkov, V.E.; and Ignat'eva, T.V. Embryotoxic effect of ethanol and products of its biotransformation in post-implanted rat embryo culture. Byull Exsp Biol Med 92(12): 725-728, 1981.

Potter, B.J.; Belling, G.B.; Mano, M.T.; and Hetzel, B.S. Experimental production of growth retardation in the sheep fetus after exposure to alcohol. Medical Journal of Australia 2:191-193, 1980.

Randall, C.L. Alcohol as a teratogen in animals. In: National Institute on Alcohol Abuse and Alcoholism. Biomedical Processes and Consequences of Alcohol Use. Alcohol and Health Monograph No. 2. DHHS Pub. No.(ADM)82-1191. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 291-307.

Randall, C.L., and Taylor, W.J. Prenatal ethanol exposure in mice: Teratogenic effects. Teratology 19:305-312, 1979.

Randall, C.L.; Taylor, W.J.; and Walker, D.W. Ethanol-induced malformations in mice. Alcoholism: Clinical and Experimental Research 1:219-224, 1977.

Randall, C.L.; Burling, T.A.; Lochry, E.A.; and Sutker, P.B. The effect of paternal alcohol consumption on fetal development in mice. Drug and Alcohol Dependence 9:89-95, 1982.

Randall, C.L.; Lochry, E.A.; Hughes, S.S.; and Sutker, P.B. Dose-response effect of prenatal alcohol exposure on fetal growth and development in mice. Substance and Alcohol Actions/Misuse 2:349-357, 1981.

Rasmussen, B.B., and Christensen, N. Teratogenic effect of maternal alcohol consumption on the mouse fetus: A histopathological study. Acta Pathologica Microbiologica Scandinavica (Section A, Pathology) 88:285-289, 1980.

Riley, E.P.; Lochry, E.A.; and Shapiro, N.R. Lack of response inhibition in rats prenatally exposed to alcohol. Psychopharmacology 62:47-52, 1979a.

Riley, E.P.; Lochry, E.A.; Shapiro, N.R.; and Baldwin, J. Response perseveration in rats exposed to alcohol prenatally. Pharmacology, Biochemistry and Behavior 10:255-259, 1979b.

Rosett, H.L. A clinical perspective on the fetal alcohol syndrome (editorial). Alcoholism: Clinical and Experimental Research 4:119-122, 1980.

Rosett, H.L., and Weiner, L. Identifying and treating pregnant patients at risk from alcohol. Canadian Medical Association Journal 125:149-154, 1981.

Rosett, H.L.; Weiner, L.; and Edelin, K.C. Strategies for prevention of fetal alcohol effects. Obstetrics and Gynecology 57:1-7, 1981.

Rosett, H.L.; Ouellette, E.M.; Weiner, L.; and Owens, E. Therapy of heavy drinking during pregnancy. American Journal of Obstetrics and Gynecology 31:41-46, 1978.

Rosett, H.L.; Weiner, L.; Lee, A.; Zuckerman, B.; Dooling, E. and Oppenheimer, E. Patterns of alcohol consumption and fetal development. Obstetrics and Gynecology 61: 539-546, 1983.

Rosett, H.L.; Snyder, P.; Sander, L.W.; Lee, A.; Cook, P.; Weiner, L.; and Gould, J. Effects of maternal drinking on neonate state regulations. Developmental Medicine and Child Neurology 21:464-473, 1979.

Russell, M. The impact of alcohol-related birth defects (ARBD) on New York State. Neurobehavioral Toxicology 2:277-283, 1980.

Russell, M., and Bigler, L.R. Screening for alcohol-related problems in an outpatient obstetric-gynecologic clinic. American Journal of Obstetrics and Gynecology 134: 4-12, 1979.

Samson, H.H., and Diaz, J. Altered development of brain by neonatal ethanol exposure: Zinc levels during and after exposure. Alcoholism: Clinical and Experimental Research 5:363-369, 1981.

Shaywitz, S.E.; Cohen, D.J.; and Shaywitz, B.A. Behavior and learning difficulties in children of normal intelligence born to alcoholic mothers. Journal of Pediatrics 96: 978-982, 1980.

Snow, M.H.L., and Tam, P.P.L. Is compensatory growth a complicating factor in mouse teratology? Nature 279:555-557, 1979.

Sokol, R.J. Alcohol-in-pregnancy: Clinical research problems. Neurobehavioral Toxicology and Teratology 2:157-163, 1980a.

Sokol, R.J. Alcohol and spontaneous abortion (letter to the editor). Lancet 2:1079, 1980b.

Sokol, R.J. Alcohol and abnormal outcomes of pregnancy. Canadian Medical Association Journal 125:143-148, 1981.

Sokol, R.J. Alcohol and pregnancy: A clinical perspective for laboratory research. Substance and Alcohol Actions/Misuse 3:183-186, 1982.

Sokol, R.J.; Miller, S.I.; and Reed, G. Alcohol abuse during pregnancy: An epidemiologic study. Alcoholism: Clinical and Experimental Research 4:135-145, 1980.

Sokol, R.J.; Miller, S.I.; and Martier, S. Identifying the alcohol abusing obstetric/gynecologic patient: A practical approach. In: National Institute on Alcohol Abuse and Alcoholism. Preventing Fetal Alcohol Effects: A Practical Guide for Ob/Gyn Physicians and Nurses. DHHS Pub. No (ADM)81-1163. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981. pp. 3-20.

Streissguth, A.P.; Herman, C.S.; and Smith, D.W. Intelligence, behavior and dysmorphogenesis in the fetal alcohol syndrome: A report on 20 patients. Journal of Pediatrics 92:363-367, 1978a.

Streissguth, A.P.; Herman, C.S.; and Smith, D.W. Stability of intelligence in the fetal alcohol syndrome: A preliminary report. Alcoholism: Clinical and Experimental Research 2:165-170, 1978b.

Streissguth, A.P.; Barr, H.M.; Martin, D.C.; and Herman, C.S. Effects of maternal alcohol, nicotine and caffeine use during pregnancy on infant mental and motor development at 8 months. Alcoholism: Clinical and Experimental Research 4:152-164, 1980.

Streissguth, A.P.; Martin, D.C.; Martin, J.C.; and Barr, H.M. The Seattle longitudinal prospective study on alcohol and pregnancy. Neurobehavioral Toxicology and Teratology 3:223-233, 1981.

Streissguth, A.P.; Darby, B.L.; Barr, H.M.; Smith, J.R.; and Martin, D.C. Comparison of drinking and smoking patterns during pregnancy over a six-year interval. American Journal of Obstetrics and Gynecology 145: 716-724, 1983.

Streissguth, A.P.; Martin, D.C.; Barr, H.M.; Sandman, B.A.; Kirchner, G.L.; and Darby, B.L. Intra-uterine alcohol exposure and attentional decrements in 4-year-old children (abstract). Alcoholism: Clinical and Experimental Research 7:122, 1983.

Sulik, K.K.; Johnston, M.C.; and Webb, M.A. Fetal alcohol syndrome: Embryogenesis on a mouse model. Science 214:936-938, 1981.

Sullivan, W.C. A note on the influence of maternal inebriety on the offspring. Journal of Mental Science 45:489- 503, 1899.

Tanaka, H.; Suzuki, N.; and Arima, M. Hypoglycemia in the fetal alcohol syndrome in the rat. Brain and Development 4:97-103, 1982.

U.S. Department of Health and Human Services. Fourth Special Report to the U.S. Congress on Alcohol and Health. DeLuca, J.R., ed. DHHS Pub. No. (ADM)81-1080. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

U.S. Department of Health, Education, and Welfare. Third Special Report to the U.S. Congress on Alcohol and Health. Noble, E.P., ed. DHEW Pub. No. (ADM)79-832. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1978.

Warner, R.H., and Rosett, H.L. The effects of drinking on offspring: An historical survey of the American and British literature. Journal of Studies on Alcohol 36:1395-1420, 1975.

Weiner, L.; Rosett, H.L.; and Edelin, K.C. Behavioral evaluation of fetal alcohol education for physicians. Alcoholism: Clinical and Experimental Research 6:230-233, 1982.

Weiner, L.; Rosett, H.L.; Edelin, K.C.; Alpert, J.J.; and Zuckerman, B. Alcohol consumption by pregnant women. Obstetrics and Gynecology 61:6-12, 1983.

West, J.R.; Hodges, C.A.; and Black, A.C., Jr. Prenatal exposure to ethanol alters the organization of hippocampal mossy fibers in rats. Science 211:957-959, 1981.

Wiener, S.G.; Shoemaker, W.J.; Koda, L.Y.; and Bloom, F.E. Interaction of ethanol and nutrition during gestation: Influence on maternal and offspring development in the rat. Journal of Pharmacology and Experimental Therapeutics 216: 372-379, 1981.

Wilson, J.G. Environment and Birth Defects. New York: Academic Press, 1973. 305 pp.

Chapter VI

Adverse Social Consequences of Alcohol Use and Alcoholism

Heavy drinking and chronic alcoholism contribute to a variety of social problems. In addition to accidents involving various modes of transportation, accidents occur in the home, at work, and during recreational activities. Alcohol use also contributes to loss of work productivity, homicide, suicide, and assaultive behaviors. In a 1982 national Gallup survey, one-third of persons interviewed said alcohol had caused problems in their families (Gallup 1982).

Research on the contribution of heavy alcohol consumption and alcoholism to social problems varies in quality. Although the causal link is sometimes weak or nonexistent, the best evidence available strongly suggests that many of these problems are much more likely to arise among alcoholics or heavy drinkers than among other persons. Moreover, the potential for some of these problems to occur may be heightened by even moderate consumption (Moore and Gerstein 1981, pp. 44-45). Since moderate drinkers outnumber heavy drinkers, moderate drinking may actually contribute substantially to social problems. Because most individuals do not believe they personally will experience drinking-related problems, it has been difficult to sensitize the public to social problems caused by moderate drinking.

Alcohol and Accidents

Traffic Accidents

Traffic accidents across the country resulted in 49,268 deaths in 1981 (USDOT 1983). Nearly 150,000 persons are permanently disabled each year in automobile accidents, and 1.8 million persons sustain injuries that restrict their activities for at least 1 full day after a crash (National Safety Council 1982). During the past decade, more than 450,000 traffic accident fatalities constituted the fifth leading overall cause of death in the United States and the leading cause of death in the 1- to 35-year-old age group (Ross 1982).

After analyzing case reports, simulated driving conditions, and epidemiologic data, researchers have consistently and unequivocally concluded that alcohol contributes significantly to traffic accidents. The higher the amount of alcohol consumed, the greater the likelihood that an accident will occur and that the accident will be serious or fatal.

In a report to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), Cameron (1977) cited 23 studies showing that at least one-third of the drivers in fatal accidents had blood alcohol concentrations (BACs) exceeding .10 percent. This effect roughly equals that in a 155-pound man who consumed at least five or six drinks or more within an hour. Estimates place the annual number of deaths in traffic accidents in which at least one driver had been drinking at 16,000 to 30,000 (Roizen 1982). Between 20 and 40 percent of people killed in these drinking-driving accidents were persons other than the drunk driver (Reed 1981).

Borkenstein and colleagues (1974) interviewed Indiana drivers about their drinking and tested their blood alcohol contents. Regardless of the frequency with which drivers reported drinking, elevated BACs increased crash probabilities. Studies comparing drivers in fatal accidents with drivers not involved in accidents in similar locations at similar times suggest that drivers with BACs above .10 percent are 3 to 15 times more likely than nondrinking drivers to be involved in a fatal crash (Cameron 1977). For young drivers, in particular, the risk of a fatal crash increases sharply with increasing BAC levels (Perrine et al. 1971; Wagenaar et al. 1981). For further discussion of this topic, see tables 4 and 5 in chapter 1 of this volume.

Because of the high risk of fatal accident involvement after heavy drinking, the risks posed by driving after moderate drinking are sometimes overlooked. According to studies in New York City (McCarroll and Haddon 1962)

and Vermont (Perrine et al. 1971), even drivers with BACs of .05 percent to .099 percent are 1.25 to 3.25 times more likely to be involved in fatal accidents than nondrinking drivers. According to the U.S. Department of Transportation (Fell 1982), while 50 percent of fatally injured drivers had BACs above .10 percent, 12 percent had elevated BACs between .01 percent and .10 percent. Reed (1981) has estimated that if all drivers in this country in 1977 were only exposed to the risk of drivers who do not drive after drinking, there would have been 24 percent fewer accidental deaths (11,700 deaths prevented) and 156,000 to 300,000 fewer injuries.

Alcohol contributes to traffic accidents by affecting cognitive and behavioral function, often in multiple ways in the same accident. Alcohol in the blood at levels above .10 percent is known to (1) lower divided attention performance, (2) reduce dynamic visual activity, (3) reduce adaptation to brightness and glare resistance recovery, and (4) reduce ability to see flickering lights, e.g., turn signals (Perrine 1974). Some researchers believe alcohol also interferes with the brain's ability to process large quantities of information at one time (Moskowitz 1974). Still others cite the sedating, fear reducing, and disinhibitory effects of alcohol on aggressiveness or self-destructiveness. Cognitive effects such as short-term memory loss or learning deficits may also contribute to accidents (Barry 1974). Those willing to drive after heavy drinking, of course, may generally engage in high risk-taking behavior and may be impulsive and careless (Jones and Joscelyn 1978). This may place them at increased risk for highway accidents regardless of their drinking behavior.

Most researchers concur that chronic heavy drinkers or alcoholics are more likely than light drinkers or nondrinkers to be involved in traffic accidents (Fell 1982). Estimates vary widely, however, on the proportion of accidents involving each category, largely because of variable criteria for diagnosing alcoholics. Klatsky et al. (1981) compared 2,015 Kaiser Permanente plan members who averaged six or more drinks daily with 6,045 light drinkers and nondrinkers matched by age, sex, race, cigarette use, and city. Those who reported drinking more than six drinks daily were three times more likely than the rest of the sample to die in a traffic accident during the subsequent 10 years.

Although persons with a previous driving-while-intoxicated (DWI) arrest run a higher accident risk than other drivers, they are involved in only a small fraction of fatal accidents. Sterling-Smith (1976) reported that of drivers known to be responsible for fatal accidents in the early 1970s in Massachusetts, only 4 percent had a previous DWI arrest, about one-tenth of those in the study with a BAC above .05 percent. The implication is that even highly successful rehabilitation programs aimed at the arrested drunk driver may influence only a small minority of drunk drivers. If the percentage of drunk drivers who are arrested increases, however, these successful rehabilitation percentages may increase.

Despite widespread awareness of its risk, drunk driving occurs relatively frequently. Researchers have estimated that at any given time 2 to 3 percent of the driving population are legally intoxicated, and that the percentage doubles at night or on weekends, the hours during which accidents are most frequent (Damkot et al. 1977; Haddon and Blumenthal 1981). As many as 20 percent of nighttime drivers randomly stopped have been found to have measurable BACs (Damkot et al. 1977). Statewide random sample surveys of nearly 1,000 adults in Massachusetts in 1981 indicated that 29 percent of drivers report driving after drinking at least four times in the prior month, and 4 percent report driving after six or more drinks at least four times a month. Males, persons who are unmarried, and those under age 25 most often reported driving after drinking heavily (Hingson et al. 1982a, 1983).

At least three reasons explain why people drive after drinking. First, a considerable number of people who drink do not know the level of drinking that makes individuals legally too intoxicated to drive. The 1981 Massachusetts survey indicated that 10 percent of the respondents who drive did not know the level of legal intoxication, and 17 percent felt that a person can drink six or more drinks without being legally too drunk to drive. Second, even though the relative risk of accident involvement for persons who drive under the influence is much higher than for nondrinkers, the probability of an accident during a trip when the driver is under the influence is still quite low, only about 2 per 1,000 trips (Ross 1982). The risk of arrest is roughly comparable, after which the drunk driver would still stand only a 50-50 chance of being punished (Jones and Joscelyn 1978; Ross 1982). Finally, driving after drinking has long been considered socially acceptable behavior. While political and social pressures have prompted 34 States to change their drunk driving laws during the past

2 years (Volpe 1982), it is not clear whether this will substantially alter public complacency about drunk driving and the frequency of its occurrence.

Pedestrian Accidents

At least 8,000 pedestrians are killed and 100,000 injured each year by motor vehicles. Research indicates measurable BACs among fatally injured pedestrians ranging from 35 to 74 percent (Blomberg et al. 1979).

Only two studies compared fatally injured pedestrians with noninjured pedestrians who passed the same spot at a similar time of day and day of week (Haddon et al. 1961; Blomberg et al. 1979). In the more recent and more extensive study (Blomberg et al. 1979), between July 1972 and March 1976, postmortem BAC results were obtained on all 86 fatally injured pedestrians taken to a New Orleans hospital. All 180 injured pedestrians taken to the same hospital between March 1975 and March 1976 were also tested. Pedestrians who passed the same site within 30 minutes of the accidents on the same day of the week and year were also stopped; 1,208 of 1,469 eligible control respondents were given blood alcohol tests and interviewed.

Thirty-six percent of the injured pedestrians had BACs over .10 percent, as did 45 percent of the pedestrians who died. Only 13 percent of controls had BACs at that level. Compared with age- and sex-matched nondrinkers, the risk of accident involvement for pedestrians was two times higher with BACs above .10 percent and five times higher for those with BACs above .20 percent. The relative risk rose rapidly as the blood alcohol concentration increased beyond .20 percent.

Driver error was less frequently the cause when the pedestrian had been drinking. Alcohol-involved accidents were more frequent among male pedestrians aged 20 to 49 and tended to cluster on weekends and at night.

Airplane Accidents

Alcohol is also a factor in aviation accidents (U.S. National Transportation Safety Board 1979). In 678 fatal plane crashes nationwide in 1979, alcohol impairment was identified in 30 pilots, most of whom had BACs above .10 percent. Because the proportion of pilots who fly after drinking and the proportion of flight time under the influence are not known, however, the relative risk of aviation accidents at various drinking levels is yet unclear.

Occupational Accidents

Work-related accidents were responsible for 13,000 fatalities in 1980, and 80,000 persons were permanently disabled, partially or totally (National Safety Council 1982). National survey data suggest that yearly 25 percent of workers sustain some sort of injury on the job (Quinn and Shepard 1974). About 35 percent of the work-related fatal accidents are represented in the traffic accident statistics already cited.

Accidents on the job are not as extensively researched as traffic accidents; less is known about their occurrence and contributory factors (including alcohol). Baker and associates (1982) indicated that in 1978, 148 Maryland workers died in job-related accidents. Blood alcohol concentration levels were obtained on 79 percent of those from whom BACs could technically have been obtained. About 11 percent of both motor vehicle fatalities and fatalities from other causes had BACs above .08 percent. In contrast, according to a national survey of workers (Quinn and Shepard 1974), only 2 percent of the working population can be expected to drink on the job on any given day. Although the types of jobs and worker characteristics in a national sample may systematically differ from those in Maryland, these data suggest that people who have fatal accidents on the job were much more likely than other employees to drink at work.

Given the well-established relationships between blood alcohol levels and poor coordination, faulty judgment, and lengthened reaction time, it is plausible that alcohol often contributes to accidents at work. Of course, the risk may well vary with the type of work.

Some data also suggest that alcoholics are more likely than other workers to experience work-related accidents, but the results have not been consistent. Shain (1982) studied one firm located in the eastern United States and found that alcoholics are two to three times more likely than other employees to be involved in work accidents, but alcoholism was not adequately defined in this study. Trice (1965) compared 72 alcoholic employees with "normal" employees and found no relation between alcoholism and accident involvement during the 5 years preceding and 1 year following diagnosis.

Additional research is needed on alcohol use and alcoholism as they affect accident involvement at work. Research priority should be given to (1) national or regional surveys to

determine the prevalence of on-the-job drinking and the incidence of accidents after drinking, (2) systematic BAC testing on all occupational fatalities, and (3) case control studies comparing alcohol use by employees involved in occupational accidents with that of employees who work at similar jobs but were not involved in accidents.

Valid data may be difficult to obtain because of legal questions concerning financial responsibility for defective products as well as worker compensation when the worker had been drinking prior to the accident. Furthermore, other characteristics that contribute to drinking on the job (job boredom, stress) could independently relate to accident involvement.

Home and Recreational Accidents

Nationwide, in 1980, 22,800 persons died and another 90,000 were permanently injured in home accidents. Falls accounted for about one-third of home accident deaths, and burns or injuries resulting directly from fires comprised another 20 percent. Outside the home, 21,000 persons died and 60,000 were permanently injured in non-motor-vehicle accidents such as falls, drownings, and other recreational accidents. From 1970 to 1980, the sharpest declines in fatal accident rates--about 25 percent--were recorded in these groupings (National Safety Council 1982).

The role of alcohol is less well understood in home and nontransportation accidents than in traffic accidents because on-the-scene investigations are less frequently conducted and most studies are undertaken in hospital emergency clinics. Moreover, because these accidents encompass a wider variety of circumstances, identifying specific causes for each accident type is more difficult. Since different researchers use different taxonomies, it is difficult to combine the results into effective generalizations.

The few studies available suggest that alcohol may contribute to some of these accidents. Wechsler et al. (1969) compared home accident admissions with emergency room admissions for other reasons, e.g., circulatory or digestive disorders. Twenty-two percent of 620 patients in home accidents had positive BACs compared with 9 percent of nonaccident patients. Eleven percent had blood alcohol concentration levels above .05 percent compared with 3 percent of nonaccident patients. The relationship was statistically significant even after adjusting for age, sex, and socioeconomic status of persons in each group.

In a review of the available literature, Wingard and Room (1977) identified only a half dozen U.S. reports since 1950 on alcohol and fatalities from falls, drowning, and fire-related injuries. Since studies showed a considerable variation in the proportion of fatal accident victims in whom alcohol was present, it is not clear whether alcohol is more likely to be involved in certain types of accidents.

Haberman and Baden (1978), in a report on 121 falling, fire, and drowning deaths in New York City between 1974 and 1975, indicated that 43 percent of such victims had blood alcohol concentrations above .10 percent. That proportion actually exceeded the proportion of motor vehicle and pedestrian accidents involving blood alcohol at that level during the same time period. Only about half the accidents in each of those categories during that time period were available for study. Yet, even if all the omitted accidents did not involve alcohol, 20 to 25 percent of the falls, burns, and drownings would still have occurred to persons with BACs above .10 percent. In contrast, on any given day one can expect only 3 percent of the population in a large urban area to consume the equivalent of five or more drinks, the amount needed to achieve a BAC of .10 percent (Hingson et al. 1981). However, the proportion of persons in similar social and demographic groups as those in accidents who consume that much has not been determined.

Alcohol's contribution to accidents may vary by type of accident. In some, such as falls, alcohol may reduce sensory motor coordination. In drownings, alcohol may contribute by increasing the risk-taking behaviors of swimmers or boaters or by reducing coordination so that capsizing is more likely. Once the person is in the water, alcohol may hasten a loss of body heat (Stanley and Siegal 1981). Alcohol may prompt smokers to fall asleep and risk cigarette fires (Levine and Radford 1977).

Some studies compare death rates from accidents of alcoholics or heavy drinkers with those of the rest of the population. When Brenner (1967), Nicholls et al. (1974), and Schmidt and de Lint (1972) compared alcoholic samples with matched age- and sex-specific populations, they found a 5 to 13 times greater risk of dying from falls among alcoholics. Schmidt and de Lint also reported a tenfold increase in death rates in fires among alcoholics. Social class and possible living environment differences between the groups were not, however, controlled in these studies. In the study of 2,015 Kaiser Permanente Health

Plan members (Klatsky et al. 1981), heavy drinkers were 2.7 times as likely as the overall sample to die in an accident (other than traffic accident) during the subsequent 10 years. Specific comparisons on the types of accident were not made and none of these studies examined alcohol consumption immediately prior to the accident.

Of course, using alcohol or being alcoholic is only one of many factors that contribute to such accidents, and its presence does not necessarily imply a causal role. Research is needed to assess when alcohol may have an independent effect beyond other factors such as age, architecture, poverty, poor housing, and smoking. The national fire survey does not query fire witnesses and victims about alcohol, even though drinkers are much more likely than nondrinkers to smoke and smoking is well known to relate to the incidence of fires (FEMA 1982). Case control studies that compare persons in falls with persons passing similar locations at similar times of day who do not fall would help establish the relative risk for intoxicated persons.

Alcohol and Crime

Homicide

In 1980, there were 22,516 murders in the United States or 9.8 per 100,000 inhabitants. The rate per 100,000 inhabitants rose 11 percent since 1976 (USDOJ 1981).

It has long been recognized that alcohol is frequently present in both perpetrators and victims. Wolfgang's landmark study (1958) in Philadelphia indicated that either the victim or the offender or both had been drinking in nearly two-thirds of the slayings he studied, and in 44 percent, both parties had been consuming alcohol.

Roizen and Schneberk (1977) identified 11 studies that reported a range of alcohol involvement in from 28 to 85 percent of arrested offenders. Greenberg's review (1981) of 28 studies indicated that a majority of victims or offenders or both drank prior to the crime. Reports of involvement varied somewhat by type of study. Studies of police reports and arrested populations identified alcohol in 66 percent of cases, whereas 9 prison studies identified its involvement in 44 percent of cases. In 4 of 5 studies reviewed by Greenberg (1981), at least 20 percent of the individuals who committed murder also had an alcoholism problem.

These findings have prompted some researchers to hypothesize a direct causal relationship between heavy alcohol consumption or alcoholism and murder. Numerous theories attempt to explain how alcohol may be directly related to violent crime (Pernanen 1981). To cite a few:

- Alcohol may reduce inhibition and release violent impulses.
- Alcohol may alter neurotransmitter activity.
- Chronic excessive alcohol use may lead to temporal lobe dysfunction, which in turn may contribute to violent behavior.

Still others argue that alcohol use contributes to violence only in the presence of such conditions as hypoglycemia, produced by poor nutrition among chronic heavy drinkers, or persistent lack of REM (rapid eye movement) sleep activity as a result of prolonged drinking. Either of these factors may produce heightened irritability among drinkers.

However plausible these theories may be, no studies to date provide clear evidence that alcohol is an independent causal factor in murder. According to Collins (1981), "the number of scientists arguing for direct and simple relations between the presence of alcohol and crime has decreased as the complexity of logic and sophistication of designs has increased." MacAndrew and Edgerton (1973), using cross-cultural analyses, suggest that behavior while intoxicated may depend more on what is considered socially acceptable while intoxicated than on disinhibitory effects.

Several researchers have also noted that some variables simultaneously contribute to both alcohol use or alcoholism and crime, possibly making the alcohol-crime relation coincidental rather than causal. For example, heavy drinking is more apt to occur in marital situations in which neither partner is satisfied or happy (Hingson et al. 1981). While such situations may also be more likely to result in murder, it is difficult to say whether alcohol and/or the underlying unhappiness contributed to such murders.

Similarly, Wolfgang (1967) has cautioned that drinking is a part of the mores of low-income young males, the group involved in most murders. But tension and frustration may also be more common among this subgroup, which in turn prompts some to commit murder as well as to drink. Also, alcohol use and vio-

lence are both more likely to be found in settings (e.g., bars) where low-income young males congregate. It is difficult to establish whether alcohol contributes to violence, or whether it at times even helps avert violence and murder by relieving tension and frustration.

Few studies in this area attempt to control for these possibly confounding factors. Of 35 studies on crime reviewed by Greenberg (1981), only 5 controlled for age, sex, and race, factors related not only to the incidence of murder but also to drinking.

Other methodologic limitations of the existing research on this topic have been discussed by Roizen and Schneberk (1977). Distinctions are seldom drawn between presence of alcohol and actual intoxication, and length of time since alcohol ingestion is rarely indicated. Data are collected at different points in the judicial process: arrest, court, and prison. The limited data available suggest that murderers who had been drinking and are caught are more likely to be convicted and hence overrepresented in prison populations (Greenberg 1981). In all studies of murder, the definition of the crime itself may be blurry; for example, manslaughter and homicide may be combined.

The presence of alcohol in the victim is not clearly and adequately understood. The few studies of victims suggest that they were frequently drinking. It is possible that drinking victims who had been drinking either lacked adequate judgment to avoid antagonizing the offender or were unable to modify the offender's anger in some way (Braucht et al. 1980). It is also possible that intoxication rendered victims less able than sober persons to defend themselves or to avoid an attack.

In studies of homicide and alcoholism, the presence of alcohol at the scene and time of the crime is seldom identified. Moreover, alcoholics are more likely to have court records such as DWI offenses, loitering, etc., and hence to be known by police. This has prompted some researchers to ask: Are alcoholic criminals more likely to get caught? (Roizen and Schneberk 1977).

It should be kept in mind that the majority of criminal offenders are not alcoholics and the majority of alcoholics never commit serious crimes (Collins 1981). Even explanations that identify alcohol as a potential contributor to violence cite other contributors as well, e.g., hereditary factors, brain dysfunction, availability of guns, media violence, and numerous other social and psychological factors (Collins 1981; Menuck and Voineskos 1981). According to Blum (1981), "Under no circumstances will alcohol be a sole cause of violence."

In sum, alcohol use is part of the lifestyle of low-income young males, those most apt to commit or be involved in murder. Even if drinking may have disinhibitory effects or long-term effects on mental functioning that in turn contribute to violence, it is unrealistic to cite alcohol as the major cause of the frustration and anger in this population that also contribute to high murder rates. Nor, however, is it realistic to dismiss alcohol as irrelevant. Alcohol may alter perceptions, cognitive performance, moods, emotions, and response capabilities and preferences. The frequent association of alcohol among murderers and their victims suggests it is more than coincidental.

It is reasonable to expect that alcohol is more likely to contribute in some types of murders than in others, e.g., quarrels among family members, friends, and acquaintances that escalate into murder. Alcohol is less likely to be involved in premeditated murders in which the perpetrator makes careful plans to avoid detection. At this point, because of inherent difficulties in studying murder and limitations in available research about alcohol and murder, one can conclude only that alcohol may be one of numerous factors that at times may independently contribute to some types of murder.

Rape

In 1980, there were 36.4 forcible rapes reported per 100,000 persons in the population, or 82,088 rapes (USDOJ 1981). This rate has steadily increased 38 percent from 1976 to 1980 in part because of changing public and law enforcement attitudes, the push from women's groups to encourage victims to report rapes, and the general increase in violent crime in the United States.

Rape is an extremely difficult crime to investigate (Rabkin 1979). Local legal codes, police enforcement, and public attitudes toward rapists and victims vary greatly by region, resulting in different reporting and recording rates. Low reporting and conviction rates limit inferences about the characteristics of rapists. In general, studies of rape draw from interviews and other data collected from apprehended rapists, who may differ from undetected rapists.

In a study of violent crime in Western Canada (Gerson and Preston 1979), 60 percent of the rapes in a 12-month period were considered to be alcohol related; either the victim or the defendant had been drinking, and the crime involved violation of an alcohol statute or occurred in a licensed alcohol establishment. Groth (1979) found that 50 percent of a group of men who raped older victims reported being high on alcohol or on alcohol and drugs.

Rada and his colleagues (1978), in a study of 382 rapists in a State mental institution, found that 81 percent of the alcoholics and 25 percent of the nonalcoholics drank before the assault. In another population, 53 percent of mentally disturbed sex offenders reported drinking heavily (Rada et al. 1978). In contrast, in a general urban population 36 percent of males can be expected to drink on any given day (Hingson et al. 1981). A more appropriate comparison would match nonrapists with rapists on other social and economic characteristics to see whether their drinking levels differ.

Few studies have examined the related question of frequency of alcoholism among rapists. Rada et al. (1978) found that 33 percent of 77 rapists had a history of alcoholism. Twenty-seven percent of 82 rapists in another group of subjects (Barnard et al. 1979) were identified as alcoholics. The proportion of alcoholics in the general population is much lower.

These studies suggest that people who commit rape are disproportionately likely to have been drinking or to be alcoholics. However, the reasons for this alcohol-rape connection are not well understood. Wilson (1981) reviewed two major theories. Disinhibition theory suggests that alcohol releases otherwise well-controlled sexual or aggressive behaviors. An alternative explanation based on social learning principles suggests that behavior after consuming alcohol is determined by past learning about the effects of alcohol on actions and by personal expectations about the consequences of a certain course of action. A social learning model of alcohol-associated rape might suggest that alcohol consumption is seen as a way to disavow responsibility for actions and thereby avoid external punishment, social disapproval, or internal guilt for attempting rape.

In conclusion, it appears that alcohol consumption and rape may be associated, but this link may have been overstated. Some rapists may actually plead drunkenness or alcoholism as a way to avoid legal responsibility for the crime. Thus, the role of alcohol in rapes is still poorly understood.

Other Crime

The relationship of alcohol to other crime is even less clear. Data on the characteristics of perpetrators should be considered with much greater caution than those of murder offenders since a lower proportion reach the attention of the police.

Fewer studies have been undertaken on alcohol involvement in other crimes than in murder. Table 1 indicates the relative alcohol involvement for these crimes in contrast to murder (Greenberg 1981). Compared with murder, the proportion of these crimes with alcohol involvement appears to be lower. Because, with the exception of aggravated assault, most of these crimes are premeditated and carried out with the intent of avoiding arrest, it is unlikely that alcohol will be as strong a potential contributor as in crimes of passion and violence.

Alcohol and the Family

Separation and Divorce

The annual divorce rate in 1977 in the United States among women over the age of 15 was 21 per 1,000. These rates have been climbing steadily since 1967 (USDHHS 1980). Evidence suggests that the rate of separation and divorce among alcoholics and their spouses is seven times that of the general population (Paolino and McCrady 1977). Forty percent of family court problems involve alcoholism in some way (Jacob and Seilhamer 1982), and it is estimated that 33 percent (Jacob and Seilhamer 1982) to 40 percent (USDHEW 1975) of intact alcoholic couples have poor marital relationships.

Alcohol is clearly associated with disrupted family functioning, but the marital and family problems may precede the alcoholism, may occur solely as a result of the alcoholic's drinking and behavior changes, or may be part of a complex interaction between preexisting weaknesses of the family or of individuals in the family and the drinking of one family member.

Family Violence

The abuse of children by their parents, and the abuse of spouses by their marital partners,

Table 1. Alcohol involvement in criminal events, by type of crime

Percentage of crime victims or offenders in whom alcohol was present during criminal event[a]	Frequency of studies							
	Homicide	Sexual offenses	Aggravated assault	Robbery	Burglary	Larceny	Auto theft	Forgery/ bad checks
0 - 10	2	-	-	-	-	1	-	-
11 - 20	4	-	1	1	1	-	-	-
21 - 30	-	2	2	-	-	-	-	-
31 - 40	2	1	-	-	2	-	-	-
41 - 50	2	3	1	-	-	1	1	1
51 - 60	4	1	-	1	1	1	1	2
61 - 70	4	1	3	2	1	1	1	-
71 - 80	2	-	-	1	-	1	-	-
81 - 90	7	-	-	-	1	-	-	-
91 - 100	1	1	1	-	-	-	-	-
Total studies[b]	28	9	8	5	6	5	3	3

[a] These percentages reflect the presence of alcohol, as defined in a variety of ways, immediately prior to or during the crime. The number upon which the percentages are based are therefore either total cases (victims) or total offenders. In studies in which drinking on the part of both victims and offenders is reported, the percentage of victims only is reported in this table.

[b] This table is based on the findings of 35 studies. The grand total does not add to 35 because some studies include data on only one type of crime, while others include two or more types of crime and therefore appear in more than one column.

Source: Greenberg 1981.

have received increasing attention in the media and in the professional literature. Self-help groups for parents who abuse their children (e.g., Parents Anonymous) and shelters for battered women have proliferated throughout the country.

The study of family violence, however, is an extremely sensitive, emotionally laden, and difficult pursuit. The definitions of abuse vary widely, and incidents of abuse are markedly unreported. Research in this area is hampered by the traditional sanctity of the family and the blurred lines between acceptable family behavior and abuse.

Most studies that have attempted to understand causes for family violence, or the links between violence and alcohol use, have sampled individuals in treatment. Such individuals represent only that fraction of the abusing population who have admitted they have problems, or whose abuse has become severe enough to come to the attention of outside authorities, who required that they undergo treatment.

Finally, many attributions of violence are based on retrospective reports of the abuser, the victim, or a third party. Recall may be faulty, making attribution of violence to drinking or drunkenness suspect. One party may place primary emphasis on drinking that another would see as immaterial, or alcohol use may be presented as an excuse for violent behavior. Aarens et al. (1977) noted in one study of domestic violence that the com-

plainant stated that the abusive party was drinking or drunk much more often than was noted by the police. Finally, alcohol consumption may be irrelevant or coincidental or may have created or contributed to a conflict that culminated in violence.

Child abuse.--This discussion does not consider child neglect or failure to provide necessary food, shelter, or medical care but instead focuses on willful commitment of injury to the abused person. A national survey conducted in 1965 revealed that 2 to 4 percent of the adults surveyed personally knew families in which child abuse had occurred in the previous year (Gil 1970). Three literature reviews concerning drinking, alcoholism, and child abuse (Aarens et al. 1977; Hamilton and Collins 1981; Orme and Rimmer 1981) identified only three studies that determined the frequency of drinking during actual episodes of child abuse. Two of these note that 12 percent of abusers were drinking at the time (Gil 1970; Thomson et al. 1971), while only 3 to 6 percent were drinking in the third study (Scott 1973).

When considering the frequency of alcohol problems or alcoholism in child abuse cases, reports range from "no association" to 38 percent of abusers' having alcohol problems. The most frequently reported figures are that between 11 and 17 percent of abuse cases involve alcoholism.

Overall, the currently available evidence does not indicate a strong association between drinking or alcoholism and child abuse. As Orme and Rimmer (1981) concluded, "When estimates of alcoholism and alcohol problems in the general population were available, the prevalence appeared to be almost identical to that in child abusers" (p.284).

Spouse abuse.--Figures on spouse abuse tend to focus almost exclusively on the abuse of women by their husbands or lovers. During 1978, 6.6 percent of murder victims were women killed by either their husbands or their lovers (USDOJ 1981). Hamilton and Collins' (1981) review of 15 studies suggested that 17 to 35 percent of divorces involve violence.

Hamilton and Collins (1981) reported that most studies cite alcoholism or excessive drinking in 45 to 60 percent of spouse abuse. Most of these reports of alcohol problems come from the female victims of the abuse. These women may exaggerate or overestimate the seriousness of their partners' drinking or may prefer to believe their mates have a drinking problem rather than accept other reasons for the abuse (Aarens et al. 1977; Hilberman 1980). Estimates of actual alcohol consumption at the time of abuse vary from 29 to 71 percent, although virtually all these figures are based on victim recall and were not verified by objective means such as BAC analyses.

Several theories have tried to explain the role of alcohol in spouse abuse. Gelles and Straus (1979) have suggested that alcohol is used as an excuse for violence because, when drunk, a person may deny responsibility for his or her actions. Denial of responsibility for actions when drinking is common in American society (Richardson and Campbell 1980). Social learning theorists (Wilson 1981) suggest that people learn to expect to behave more aggressively when drinking and therefore do so, even if the alcohol itself does not have a direct disinhibitory effect on their behavior. These two models are in direct contrast to disinhibition theory, which suggests that alcohol directly disinhibits people so that they express their real, underlying aggressive impulses. A fourth model suggests an interactive relationship between drinking and violence (Gelles 1972; Pernanen 1976). Arguments about a husband's drinking may escalate into arguments about many areas of marital problems. The alcohol may diminish the drinker's ability to reason and to control his behavior, resulting in a growing conflict that may culminate in violence.

Child Functioning in Alcoholic Families

The complexity of individual, family, and social factors that interact in a child's development makes it difficult to attribute a child's particular problems or personality solely to a parent's alcoholism. The study of children of alcoholics is further complicated by the methodologies usually employed. Children in treatment often form the basis of research samples, but they reflect only the fraction whose problems are serious enough to come to the attention of treatment agencies and who are able to find such agencies. Children whose parents are in alcoholism treatment are another common yet not fully representative sample, as many people with serious drinking problems never reach treatment (Hingson et al. 1981, 1982b). Attempting to gain access to children and their families who are not connected to the treatment or social services system, however, raises diagnostic and ethical issues. When asked about parents'

drinking, for example, a child may feel he or she is betraying the parent or may fear retaliation and therefore minimize parental drinking. Even if the situation is accurately identified, obtaining parental permission for the child to participate in a research study may be difficult. Ethical questions arise also if such children in the course of a study become labeled by a social institution (e.g., their school) as socially deviant by virtue of being the children of alcoholics.

Woodside (1982) has reviewed the available data on children of alcoholics. Hyperkinesis has been suggested as one consequence of parental alcoholism. Although early studies suggested that alcoholism was twice as frequent among parents of hyperkinetic children as among normal controls, more recent data fail to support this finding (Morrison 1980; Stewart et al. 1980). Children with at least one alcoholic parent are more likely to have a childhood history of school problems and antisocial behavior than other children (Sher and McCrady in press). Other studies reviewed by Woodside (1982) have found lower self-esteem, more emotional detachment, more anxiety symptoms, more social aggression, or more psychosomatic symptoms (such as headaches or stomach aches) among children of alcoholic parents than among control children. Most of these associations have not been replicated, however, and do not explore what mechanism may lead to the childhood problems or what protects some children from such problems.

Summaries of unstructured or semistructured interviews with children of alcoholics (Cork 1969) suggest that these children feel rejected by their parents, guilty or somehow responsible for the parent's alcoholism, resentful of the alcoholic parent, and in constant fear. However, most of these studies focus on the casualties of alcoholism--the children in trouble. One notable exception sought to understand what factors spare certain children (Wolin et al. 1980). They found that alcoholic families that maintained some predictable structures, particularly around the observance of family rituals (at meals, holidays, etc.), were less likely to produce alcoholic offspring than families with disrupted family rituals.

Alcohol and Suicide

About 27,000 Americans commit suicide each year (Hendin 1982), but 10 times as many persons make unsuccessful suicide attempts. The overall rate of suicide, at 12.5 per 100,000 persons, remained fairly stable from the 1940s to the 1960s and has increased only slightly since then. Suicide among young people 15 to 24 years of age has increased dramatically, however, by 250 percent among young women and more than 300 percent among young men. There are 100 to 200 suicide attempts for every completed suicide of a high school youth.

The other high-risk population group includes white men over 45 years of age, who commit 30 percent of all suicides each year, even though they represent only 10 percent of the population. Men who are alone or have suffered recent losses are at particular risk. Black men are at their highest risk for suicide between the ages of 20 and 34, rather than when they are older (Hendin 1982).

In some situations, alcoholism may contribute to a number of problems that may in turn precipitate suicide. Separation and divorce rates are high among alcoholics (Paolino et al. 1978). Depression is common among alcoholics during prolonged drinking bouts as well as during some phases of alcohol withdrawal, and alcoholism also causes numerous debilitating and life-threatening medical problems; suicide may become a response to any of these problems.

Because suicide has many causes, however, it is difficult to discern the contributory role of alcoholism when it coexists with other problems. As many as 25 percent of female alcoholics, for example, have diagnosable depression (Schuckit and Morrissey 1979). If such a patient commits suicide, it is impossible to determine to what the suicide should be ascribed--depression or alcoholism.

Individuals use alcohol in an attempt to cope with life problems. A person facing a divorce, the death of a parent, or a serious illness may drink and, in fact, may develop a serious drinking problem. If this person commits suicide, is the suicide a result of the alcohol abuse or of the original life problem?

A number of problems with research methods further muddy the waters. Social pressures often lead to underreporting of suicide, and family members may be reluctant to acknowledge the alcoholism of a deceased relative, thus obscuring the suicide-alcoholism association. Diagnosing alcoholism based only on survivors' reports is also difficult, especially when attempting to distinguish between alcoholism and other psychological disorders. Blood alcohol levels are not always determined when someone dies. Finally, the assessment of intent of a death is sometimes problematic.

For example, a person who dies from combined drug and alcohol ingestion may have planned his or her death, or may have been unaware of the way the substances could potentiate each other. Likewise, a person who dies in a single-car accident after drinking might have deliberately caused the accident or may have simply lost control of the vehicle.

Keeping in mind these research limitations, the Fourth Special Report (USDHHS 1981) cited studies indicating between 15 and 64 percent of suicide attempters and up to 80 percent of suicides had been drinking at the time of the attempt. The wide range of percentages makes it difficult to assess whether drinking is in fact causally linked with attempts. A review of violent deaths in the Cleveland area (Ford et al. 1979) found alcohol present in 25 percent of suicide victims. Of course, determining whether drinking is independently associated with suicide would require identifying populations of similar socioeconomic status, age, race, and sex as those who commit suicide. It is particularly important to compare populations with similar sociodemographic characteristics, as suicides occur disproportionately among the young and among older single males. The presence of alcohol in the blood stream of a suicide attempter at the time of the act provides insufficient data to conclude that alcohol is independently related to the attempt. Evidence is available that alcoholism or a history of drinking problems is more common among suicide attempters. Roizen (1982) indicates that most studies reported that more than 10 percent of attempters and completers had drinking problems.

Aarens et al. (1977) provide stronger data, comparing the proportion of problem drinkers or alcoholics in a random sample survey with Beck and associates' (1975) sample of suicide attempters in two large metropolitan hospitals. The survey data were standardized by age, sex, and marital status to match the suicide population. These data indicated that suicide attempters were four to six times more likely than the general population to report being problem drinkers or alcoholics.

Several studies have also shown that, as a group, alcoholics are more likely over the course of their lifetimes to commit suicide. Reviewing reports from 1935 to 1970, Miles (1977) estimated that 15 percent of alcoholics ultimately complete suicide. Another review suggests that 6 to 12 percent of alcoholics commit suicide, compared with 1 percent of the population. Klatsky et al. (1981) reported that persons who consume more than six drinks a day as a group were twice as likely to die from suicide over a 10-year followup period than age- and sex-matched light drinkers and abstainers. It was not indicated whether these people were drinking at the time, but suicidal actions are more likely to be damaging when people have been drinking; combinations of alcohol with other drugs often have greater lethal potential (Eckardt et al. 1981).

Economic Costs of Alcohol Abuse

Alcohol and Work Productivity

Foregone work productivity is widely accepted to be an important component of the costs of alcohol abuse. The proliferation of occupationally based alcoholism programs may in part be attributed to increased employer awareness of excessive alcohol use and compromised job performance. No one has been able to precisely identify the worker productivity costs of alcohol abuse; the majority of studies have examined simple measures such as absenteeism.

A study of alcohol problems in seven railroad companies examined absenteeism as well as several empirical measures of lost productivity. Problem drinkers had almost twice the absenteeism of other workers and cost the company an estimated $3.1 million, assuming 5.2 extra days of absence per year for the 8,670 employees for whom adequate attendance records were available and based on an average employee salary of $18,000 (Mannello 1979).

Cost-benefit studies of occupational alcoholism programs generally support the claim that productivity losses attributable to alcoholic employees can be reduced. These studies generally focus on absenteeism rates among a treated group of alcoholic workers before and after an intervention. For example, Wood (1980) suggested that an occupational alcoholism program sponsored by New York Telephone Company saved the firm $1.5 million, assuming that untreated alcoholics would have been absent 20 days a year (and also that they would have incurred $2,000 in extra treatment costs). Jones (1977) attributed to Kennecott Copper Company's alcoholism program a 52-percent improvement in attendance, on average, among the 150 men who spent 12.7 months in treatment. Saxe et al. (1983) have recently reviewed similar studies of programs in the Philadelphia fire and police forces

(Jones and Vischi 1979), General Motors, and the U.S. Air Force (Orvis et al. 1981). All the studies indicate that reduced absences and cost-effectiveness are associated with those programs.

These studies focus primarily on absenteeism and illness costs (not productivity or working days), and they lack adequate controls that would suggest causal inferences. They explore only identified alcoholic employees and leave unresolved the crucial question of how these employees would have fared in the absence of treatment. Whether problem drinking causes substandard job performance or, conversely, substandard, unproductive, and hence unrewarded job performance contributes to problem drinking remains unanswered. Development of more precise estimates concerning the amount of work productivity lost because of drinking and the proportion that can be regained if employees with problems are identified and offered assistance should be a research priority in the 1980s.

Estimating the Costs of Alcohol Abuse

Given the numerous social problems associated with or caused by alcohol abuse, some attempts have been made to quantify its economic costs to society. Two major estimation procedures have been used. The population-specific approach (Berry and Boland 1977; Berry et al. 1977) compared per capita health care costs of alcohol abusers with those of nonabusers and multiplied the difference by an estimate of the prevalence of alcohol abuse, yielding a total cost of $42.8 billion in 1975. This approach has been criticized because it fails to make corrections for other health risks more common among heavy drinkers. This would tend to inflate the estimates (Cruze et al. 1981).

The alternative approach identifies specific events or illnesses associated with alcohol abuse. For example, in calculating treatment costs, the illness-specific approach includes all expenditures for illnesses attributable solely to alcohol abuse and, for illnesses with multiple causes, only those expenditures that can be ascribed to alcohol abuse. This system would tend to produce a more conservative estimate.

Using this latter approach on 1977 data, Cruze et al. (1981) estimated the national economic costs of alcohol abuse at $49.4 billion. "Direct core costs" (an estimated $6.4 billion in 1977) are expenditures for hospitalization, outpatient care, professional services, drugs and sundries, and other outlays involved in the diagnosis, treatment, continuing care, rehabilitation, and terminal care for alcohol-related illness and trauma. "Indirect core costs" (estimated for 1977 at $36.8 billion) reflect the losses of productivity associated with alcohol-related morbidity ($26.1 billion) and mortality ($10.7 billion). Table 2 specifies the components of direct and indirect core costs.

"Other related costs," $6.2 billion, include costs associated with motor vehicle crashes and fires and a proportionate share of society's expenditures for administering the systems of criminal justice, social welfare, fire protection, and highway safety. Also counted are productivity foregone by family and friends of alcoholics, productivity lost by 83,700 individuals in prisons in 1977 for crimes caused by alcohol abuse, and losses associated with automobile accidents experienced by individuals other than crash victims. Table 3 summarizes the breakdown of these other related costs.

Cruze et al. (1981) specified that when data are limited or unavailable, their estimates tend to err on the conservative side. When causal relations are imperfectly demonstrated between alcohol abuse and associated economic costs, on the other hand, their estimates tend to overstate the real costs. The issue of establishing causality was flagged by an advisory panel as "one of the most important factors in carrying out this study.... Failure to recognize the difference between causality and association will lead to unrealistically high estimates of the cost to society of alcohol abuse" (Cruze et al. 1981, p.D-3). The investigators nonetheless contend that, overall, their estimates "lean strongly in the conservative direction" (Cruze et al. 1981, p.6-1).

It is generally recognized that the total burden on society of alcohol abuse and alcoholism is substantially greater if social costs are considered. These include the pain and suffering of the alcohol abuser's family and a host of medical, psychological, and social consequences that a full accounting of costs would ultimately have to include in one way or another. Few studies do more than grant that these intangible costs would add billions of dollars to the overall economic costs to society, assuming they could be measured accurately in monetary terms (Cruze et al. 1981).

Nor has previous research ventured far into the analysis of the benefits of alcohol consumption, which from the standpoint of public

Table 2. Estimated core costs for alcohol abuse, 1977
(in $ millions)

Total core costs	$43,161
Direct	$ 6,372
Treatment	5,637
Alcohol-abuse-specific illness --specialty setting	707
Alcohol-abuse-specific illness --general setting	2,001
Alcohol-abuse-related illness categories	1,711
Gastrointestinal tract	220
Liver disease	181
Nervous system	6
Heart	17
Endocrine system	608
Nutritional deficiency	108
Cancer	171
Mental disorder	293
Infectious disease	107
Alcohol-abuse-related trauma	1,217
Support	735
Research	28
Training and education	225
Construction	193
Health insurance administration	289
Indirect	$36,789
Mortality	10,715
Direct primary causes--alcohol psychosis, alcoholism, alcoholic cirrhosis of liver, alcohol poisoning	2,617
Direct secondary causes--cirrhosis of liver-other, malignant primary liver neoplasms, other malignant neoplasms of gastrointestinal tract, pancreatitis, respiratory tuberculosis, other associated diseases	1,063
Indirect causes--motor vehicle crashes, falls, fires, other accidents, homicides, suicides	7,035
Morbidity	26,074
Lost productivity	23,593
Males	20,178
Females	3,415
Lost employment	2,481
Trauma	545
Residential treatment	328
Long-term disability	1,608

Source: Cruze et al. 1981.

policy could be considered relevant. Apart from the personal pleasures that prompt so many people to drink in the first place, the alcoholic beverage industry does make a substantial contribution to the economy. The Distilled Spirits Council of the United States, Inc., an association of producers, importers, and other industry representatives, reports that the industry paid $15.7 billion in 1981 in taxes and other fees to Federal, State, and local governments and employed 826,000 people in 400,000 firms (DISCUS 1982). Additionally, as Gerstein (1981) points out, sales of alcoholic beverages provide not only contributions to government revenues and jobs in the economy, but also an important profit margin for many businesses.

The question for our society seems to be not whether the benefits outweigh the costs, but rather what can be done to reduce the considerable expense of alcohol abuse in terms of human lives, illness, and suffering.

Summary

In 1977, the last year for which there are reliable estimates, alcohol cost the Nation approximately $50 billion--about $26 billion in lost employment and productivity, $17 billion in health care, and $7 billion in property loss and crime. Although the costs are almost certainly much higher now after 5 years of inflation and sharply increased health care costs, alcohol's impact transcends monetary loss. In many fatalities, alcohol is an accessory before the fact.

Traffic accidents, especially those involving alcohol, continue to be a major problem in our society. According to one estimate, if no drivers drank in 1977, almost 12,000 deaths and perhaps 300,000 injuries would have been prevented. Drivers who drink in excess of the legal intoxication level are 3 to 15 times as likely as nondrinking drivers to be involved in a fatal crash. Even moderate drinking at legal levels can increase the likelihood of fatal accidents. Furthermore, pedestrians killed in traffic accidents are 3 times more likely to be intoxicated than noninjured pedestrians.

Although accidents in the home and workplace have not been as extensively researched as traffic accidents, evidence is ample and growing that alcohol contributes significantly to their incidence and severity. People who drink on the job are much more likely than their coworkers to have fatal accidents at work. Results indicate that alcoholics and

Table 3. Estimated other related costs for alcohol abuse, 1977 (in $ millions)

Total other related costs	$ 6,213
Direct	$ 4,441
Motor vehicle crashes	1,782
Crime	1,685
Public criminal justice system	1,479
Law enforcement	313
Legal and adjudication	139
Corrections	1,027
Private criminal justice system	191
Law enforcement	184
Legal and adjudication	7
Corrections	-
Property loss/damage	15
Social welfare programs	142
Fire losses	319
Fire protection	482
Highway safety	31
Indirect	$ 1,772
Crime careers	-
incarceration	1,418
Homicide	276
Felonious assault	120
Robbery	46
Burglary	49
Drug laws	0
Driving under the influence	287
Liquor laws	158
Public drunkenness	461
Other	21
Motor vehicle crashes	354

Source: Cruze et al. 1981.

heavy drinkers tend to be involved in fatal falls, drownings, and fires.

More alcoholics and heavy drinkers than abstainers are involved in homicides, as both victims and offenders. The alcohol association is somewhat weaker for other crimes such as rape, theft, robbery, and assault. While there are some statistical links between alcohol and crime, factors other than alcohol may explain the relationship.

Heavy drinking seems to affect family stability profoundly. In families with at least one alcoholic spouse, the rate of separation and divorce is seven times that of the general population. Although some researchers have speculated that the incidence of child abuse and spouse abuse may be alcohol-related, reliable data are difficult to collect. Suicides are higher among alcoholics, but drinking may be a result of depression or other problems that in turn lead to suicide.

More carefully designed studies are required to establish unequivocally the potential adverse consequences of alcohol. Meanwhile, there is clear reason for concern about the social effects of excessive alcohol consumption.

References

Aarens, M.; Cameron, T.; Roizen, J.; Roizen, R.; Room, R.; Schneberk, D.; and Wingard, D. Alcohol, Casualties and Crime. Alcohol, Casualties and Crime Project Final Report. Report No. C-18. Berkeley: Social Research Group, University of California, 1977. 709 pp.

Baker, S.P.; Samkoff, J.S.; Fisher, R.S.; and Van Buren, C.B. Fatal occupational injuries. Journal of the American Medical Association 248(6): 692-697, 1982.

Barnard, G.W.,; Holzer, C.; and Vera, H. Comparison of alcoholics and nonalcoholics charged with rape. Bulletin of the American Academy of Psychiatry and the Law 7:432- 440, 1979.

Barry, H. Motivational and cognitive effects of alcohol. In: National Highway Traffic Safety Administration. Alcohol, Drugs, and Driving, Perrine, M.W., ed. Report No. DOT HS-801 096. Washington, D.C.: NHTSA, 1974. pp. 71-105. NTIS No. PB-232-111.

Beck, A.T.; Kovacs, M.; and Weissman, A. Hopelessness and suicidal behavior: An overview. Journal of the American Medical Association 234(11):1146-1149, 1975.

Berry, R.E., Jr., and Boland, J.P. The Economic Cost of Alcohol Abuse. New York: The Free Press, 1977. 200 pp.

Berry, R.E., Jr.; Boland, J.P.; Smart, C.N.; and Kanak, J.R. The Economic Cost of Alcohol Abuse — 1975. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1977. 222 pp. NTIS No. PB-278-606.

Blomberg, R.D.; Preusser, D.F.; Hale, A.; and Ulmer, R.G. A Comparison of Alcohol Involvement in Pedestrians and Pedestrian Casualties. Report No. DOT HS-805 249. Washington, D.C.: National Highway Traffic Safety Administration, 1979. NTIS No. PB80-166275.

Blum, R.H. Violence, alcohol and setting: An unexplored nexus. In: Collins, J.J., Jr., ed. Drinking and Crime: Perspectives on the Relationships Between Alcohol Consumption and Criminal Behavior. New York: Guilford Press, 1981. pp. 110-142.

Borkenstein, R.F.; Crowther, R.F.; Shumate, R.P.; Ziel, W.B.; and Zylman, R. The role of the drinking driver in traffic accidents (The Grand Rapids study). Blutalkohol 11(Supplement 1):1-132, 1974.

120

Braucht, G.N.; Loya, F.; and Jamieson, K.J. Victims of violent death: A critical review. Psychological Bulletin 87(2):309-333, 1980.

Brenner, B. Alcoholism and fatal accidents. Quarterly Journal of Studies on Alcohol 28 (3):517-528, 1967.

Cameron, T. Alcohol and traffic. In: Aarens, M.; Cameron, T.; Roizen, J.; Roizen, R.; Room, R.; Schneberk, D.; and Wingard, D. Alcohol, Casualties and Crime. Alcohol, Casualties and Crime Project Final Report. Report No. C-18. Berkeley: Social Research Group, University of California, 1977. pp. 120-288.

Collins, J.J., Jr. Alcohol use and criminal behavior: An empirical, theoretical, and methodological overview. In: Collins, J.J., Jr., ed. Drinking and Crime. Perspectives on the Relationships Between Alcohol Consumption and Criminal Behavior. New York: Guilford Press, 1981. pp. 288-316.

Cork, M. The Forgotten Children. Toronto: Addiction Research Foundation, 1969.

Cruze, A.M., Harwood, H.J.; Kristiansen, P.L.; Collins, J.J.; and Jones, D.C. Economic Costs to Society of Alcohol and Drug Abuse and Mental Illness -- 1977. Rockville, Md.: Alcohol, Drug Abuse, and Mental Health Administration, 1981. 98 pp.

Damkot, D.K.; Toussie, S.R.; Akley, N.R.; Geller, H.; and Whitmore, D. On the Road Driving Behavior and Breath Alcohol Concentration. Report No. DOT HS-802 264. Washington, D.C.: National Highway Traffic Safety Administration, 1977. 230 pp.

Distilled Spirits Council of the United States, Inc. DISCUS Facts Book 1981. Washington, D.C.: DISCUS, 1982.

Eckardt, M.J.; Harford, T.C.; Kaelber, C.T.; Parker, E.S.; Rosenthal, L.S.; Ryback, R.S.; Salmoiraghi, G.C.; Vanderveen, E.; and Warren, K.R. Health hazards associated with alcohol consumption. Journal of the American Medical Association 246(6):648- 666, 1981.

Federal Emergency Management Agency. Fire in the United States: Deaths, Injuries, Dollar Loss, and Incidents at the National, State, and Local Levels in 1978. 2d ed. Report No. FEMA-22. Washington, D.C.: FEMA, July 1982.

Fell, J.C. Alcohol Involvement in Traffic Accidents: Recent Estimates From the National Center for Statistics and Analyses. NHTSA Technical Report No. DOT HS-806 269. Washington, D.C.: National Highway Traffic Safety Administration, 1982. 27 pp.

Ford, A.B.; Rushforth, N.B.; Rushforth, N.; Hirsch, C.S.; and Adelson, L. Violent death in a metropolitan county. II. Changing patterns in suicides (1959-1974). American Journal of Public Health 69(5):459-464, 1979.

Gallup, G. Alcohol Abuse: A Problem in One of Three American Families. Princeton, N.J.: The Gallup Poll, November 13, 1982.

Gelles, R.J. The Violent Home: A Study of Physical Aggression Between Husbands and Wives. Beverly Hills: Sage Publications, 1972. 230 pp.

Gelles, R.J., and Straus, M.A. Determinants of violence in the family: Toward a theoretical integration. In: Burr, W.R.; Hill, R.; Nye, F.D.; and Reiss, I.L., eds. Contemporary Theories About the Family. New York: The Free Press, 1979. pp. 549-581.

Gerson, L.W., and Preston, D.A. Alcohol consumption and the incidence of violent crime. Journal of Studies on Alcohol 40(3):307-312, 1979.

Gerstein, D.R. Alcohol use and consequences. In: Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. pp. 182-224.

Gil, D.G. Violence Against Children: Physical Abuse in the United States. Cambridge, Mass.: Harvard University Press, 1970.

Greenberg, S.W. Alcohol and crime: A methodologic critique of the literature. In: Collins, J.J., Jr., ed. Drinking and Crime: Perspectives on the Relationships Between Alcohol Consumption and Criminal Behavior. New York: Guilford Press, 1981. pp. 70-109.

Groth, A.N. Older rape victim and her assailant. Journal of Geriatric Psychiatry 11:203-215, 1979.

Haberman, P.W., and Baden, M.M. Alcohol, Other Drugs and Violent Death. New York: Oxford University Press, 1978. 134 pp.

Haddon, W.; Valien, P.; McCarroll, J.R.; and Umberger, C.J. A controlled investigation of the characteristics of adult pedestrians fatally injured by motor vehicles in Manhattan. Journal of Chronic Diseases 14(6): 655-678, 1961.

Haddon, W., and Blumenthal, M. Foreword. In: Ross, H.L. Deterring the Drinking Driver. Legal Policy and Social Control. Lexington, Mass.: Lexington Books, 1981. pp. xiii-xxiii.

Hamilton, C.J., and Collins, J.J., Jr. The role of alcohol in wife beating and child abuse: A review of the literature. In: Collins, J.J., Jr., ed. Drinking and Crime: Perspective on the Relationships Between Alcohol Consumption and Criminal Behavior. New York: Guilford Press, 1981. pp. 253-287.

Hendin, H. Suicide in America. 1st ed. New York: W.W. Norton, 1982. 252 pp.

Hilberman, E. Overview: The "wife-beater's wife" reconsidered. American Journal of Psychiatry 137:1336-1347, 1980.

Hingson, R.; Heeren, T.; Kovenock, D.; Mangione, T.; Meyers, A.; Morelock, S.; Mucatel, M.; and Scotch, N. Impact of Maine's 1981 Operating Under the Influence Legislation. Submitted for publication, 1983.

Hingson, R.; Heeren, T.; Mangione, T.; Morelock, S.; and Mucatel, M. Teenage driving after using marijuana or drinking and traffic accident involvement. Journal of Safety Research 13(1): 33-37, 1982a.

Hingson, R.; Mangione, T.; Meyers, A.; and Scotch, N. Seeking help for drinking problems: A study in the Boston metropolitan area. Journal of Studies on Alcohol 43(3): 273-288, 1982b.

Hingson, R., Scotch, N.; Barrett, J.; Goldman, E.; and Mangione, T. Life satisfaction and drinking

practices in the Boston metropolitan area. Journal of Studies on Alcohol 42(1):24-37, 1981.

Jacob, T., and Seilhamer, R. The impact on spouses and how they cope. In: Orford, J., and Harwin, J., eds. Alcohol and the Family. New York: St. Martin's Press, 1982. pp. 114- 126.

Jones, K.R., and Vischi, T.R. Impact of alcohol, drug abuse and mental health treatment on medical care utilization: A review of the research literature. Medical Care 17(12, Supplement):1-82, 1979.

Jones, O. Kennecott's INSIGHT Program. In: Schramm, C.J., ed. Alcoholism and its Treatment in Industry. Baltimore: Johns Hopkins University Press, 1977. pp. 76-81.

Jones, R.K., and Joscelyn, K.B. Alcohol and Highway Safety 1978: A Review of the State of Knowledge. Report No. DOT HS803 764. Washington, D.C.: National Highway Traffic Safety Administration, 1978. 123 pp.

Klatsky, A.; Friedman, G.; and Sieglaub, A. Alcohol and mortality: A ten-year Kaiser Permanente experience. Annals of Internal Medicine 95(2): 139-145, 1981.

Levine, M.S., and Radford, E.P. Fire victims: Medical outcomes and demographic characteristics. American Journal of Public Health 67(11):1077-1080, 1977.

MacAndrew, C., and Edgerton, R.B. Drunken Comportment: A Social Explanation. Chicago: Aldine Publishing Co., 1973. 197 pp.

Mannello, T.A. Problem Drinking Among Railroad Workers: Extent, Impact and Solutions. Monograph Series No. 4. Washington, D.C.: University Research Corporation, 1979. 69 pp.

McCarroll, J.R., and Haddon, W. A controlled study of fatal automobile accidents in New York City. Journal of Chronic Diseases 15: 811-826, 1962.

Menuck, M., and Voineskos, G. The etiology of violent behavior: An overview. General Hospital Psychiatry 3(1):37-47, 1981.

Miles, C.P. Conditions predisposing to suicide: A review. Journal of Nervous and Mental Diseases 164(4):231-246, 1977.

Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. 463 pp.

Morrison, J. Adult psychiatric disorders in parents of hyperactive children. American Journal of Psychiatry 137:825-827, 1980.

Moskowitz, H. Alcohol influences upon sensory motor function, visual perception, and attention. In: National Highway Traffic Safety Administration. Alcohol, Drugs, and Driving, Perrine, M.W., ed. Report No. DOT HS-801 096. Washington, D.C.: NHTSA, 1974. pp. 49-69. NTIS No. PB-232-111.

National Safety Council. Accident Facts 1981. Chicago: NSC, 1982.

Nicholls, P.; Edwards, G.; and Kyle, E. Alcoholics admitted to four hospitals in England: General and cause specific mortality. Quarterly Journal of Studies on Alcohol 35(3):841-855, 1974.

Orme, T.C., and Rimmer, J. Alcoholism and child abuse. A review. Journal of Studies on Alcohol 42(3):273-287, 1981.

Orvis, B.R.; Asmor, D.J.; Williams, C.E.; Barras, A.J.; and Schwarzbach, D.S. Effectiveness and Cost of Alcohol Rehabilitation in the U.S. Air Force. Report No. R-2813-AF. Washington, D.C.: U.S. Air Force, 1981. 216 pp. NTIS No. ADA-112-787.

Paolino, T.J., Jr., and McCrady, B.S. The Alcoholic Marriage: Alternative Perspectives. New York: Grune & Stratton, 1977. 211 pp.

Paolino, T.J., Jr.; McCrady, B.S.; and Diamond, S. Statistics on alcoholic marriages: An overview. International Journal of Addictions 13(8):1283-1293, 1978.

Pernanen, K. Alcohol and crimes of violence. In: Kissin, B., and Begleiter, H., eds. Social Aspects of Alcoholism. The Biology of Alcoholism, Vol. 4. New York: Plenum Press, 1976. pp. 351-444.

Pernanen, K. Theoretical aspects of the relationship between alcohol use and crime. In: Collins, J.J., Jr., ed. Drinking and Crime. Perspectives on the Relationships Between Alcohol Consumption and Criminal Behavior. New York: Guilford Press, 1981. pp. 1-69.

Perrine, M.W. Alcohol influences upon driving related behavior: A critical review of laboratory studies of neurophysiological, neuromuscular, and sensory activity. In: National Highway Traffic Safety Administration. Alcohol, Drugs, and Driving, Perrine, M.W., ed. Report No. DOT HS-801 096. Washington, D.C.: NHTSA, 1974. pp. 13-48.

Perrine, M.W.; Waller, J.A.; and Harris, L.S. Alcohol and Highway Safety: Behavioral and Medical Aspects. Report No. DOT HS-800 600. Washington, D.C.: National Highway Traffic Safety Administration, 1971. 308 pp.

Quinn, R., and Shepard, L. The 1972-1973 Quality of Employment Survey: A Report to the Employment Standards Administration. Washington, D.C.: U.S. Department of Labor, 1974.

Rabkin, J.G. The epidemiology of forcible rape. American Journal of Orthopsychiatry 49:634-647, 1979.

Rada, R.T.; Kellner, R.; Laws, D.R.; and Winslow, W.W. Drinking, alcoholism and the mentally disordered sex offender. Bulletin of the American Academy of Psychiatry and the Law 6:296-300, 1978.

Reed, D.S. Reducing the costs of drinking and driving. In: Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. pp. 336-387.

Richardson, D.C., and Campbell, J.L. Alcohol and wife abuse: The effect of alcohol on attributions of blame for wife abuse. Personality and Social Psychology Bulletin 6 (1):51-56, 1980.

Roizen, J., and Schneberk, D. Alcohol and crime. In: Aarens, M.; Cameron, T.; Roizen, J.; Roizen, R.; Room, R.; Schneberk, D.; and Wingard, D. Alcohol, Casualties and Crime. Alcohol, Casualities and Crime Project Final Report. Report No. C-18. Berkeley: Social Research Group,

University of California, 1977. pp. 289-465.

Roizen, J. Estimating alcohol involvement in serious events. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM) 82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp.179- 219.

Ross, H.L. Deterring the Drinking Driver: Legal Policy and Social Control. Lexington, Mass.: Lexington Books, 1982. 129 pp.

Saxe, L.; Dougherty, D.; Esty, K.; and Fine, M. Effectiveness and Costs of Alcoholism Treatment. Health Technology Case Study 22. Report No. OTA-HCS-22. Washington, D.C.: Congress of the United States, Office of Technology Assessment, 1983. 108 pp.

Schmidt, W., and de Lint, J. Cause of death of alcoholics. Quarterly Journal of Studies on Alcohol 33(1):171-185, 1972.

Schuckit, M.A., and Morrissey, E.R. Psychiatric problems in women admitted to an alcoholic detoxification center. American Journal of Psychiatry 136:611-617, 1979.

Scott, P.D. Fatal battered baby cases. Medicine, Science and the Law 13(3):197-206, 1973.

Shain, M. Alcohol, drugs and safety: An updated perspective on problems and their management in the workplace. Accident Analysis and Prevention 14(3):239-246, 1982.

Sher, K.J., and McCrady, B.S. The MacAndrew Alcoholism Scale: Severity of alcohol abuse and parental alcoholism. Addictive Behaviors, in press.

Stanley, R.J., and Siegal, G.P. Death by drowning: An overview. Minnesota Medicine 64(5):295-297, 1981.

Sterling-Smith, R.S. Psychosocial Identification of Drivers Responsible for Fatal Vehicular Accidents in Boston. Part I. Report No. DOT HS-801 915. Washington, D.C.: National Highway Traffic Safety Administration, 1976.

Stewart, M.A.; DeBlois, C.S.; and Cummings, C. Psychiatric disorder in the parents of hyperactive boys and those with conduct disorder. Journal of Child Psychology and Psychiatry 21: 283-292, 1980.

Thomson, E.M.; Paget, N.W.; Bates, D.W.; Mesch, M.; and Putnam, T.I. Child Abuse: A Community Challenge. Buffalo: Stewart Press, 1971. 169 pp.

Trice, H.M. Alcoholic employees: A comparison of psychotic, neurotic, and "normal" personnel. Journal of Occupational Medicine 17(3):94-99, 1965.

U.S. Department of Health and Human Services. National Estimates of Marriage Dissolution and Survivorship: United States Vital Statistics. DHHS Pub. No. (PHS) 81- 1403. Series No. 3, Vol. 19. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1980.

U.S. Department of Health and Human Services. Fourth Special Report to the U.S. Congress on Alcohol and Health. DeLuca, J.R., ed. DHHS Pub. No. (ADM)81-1080. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

U.S. Department of Health, Education, and Welfare. Second Special Report to the U.S. Congress on Alcohol and Health. Chafetz, M.E., ed. DHEW Pub. No. (ADM)75-212. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1975.

U.S. Department of Justice, Federal Bureau of Investigation. Crime in the United States. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

U.S. Department of Transportation. United States Fatal Accident Reporting System. DOT HS 806 251, Washington, D.C.: the Department, Jan. 1983.

U.S. National Transportation Safety Board. Briefs of Accidents as a Cause/Factor: U.S. General Aviation. Washington, D.C.: U.S. NTSB, 1979. NTIS No. PB-82-138-492.

Volpe, J., Chairman. An Interim Report to the Nation of the President's Commission on Drunk Driving. Washington, D.C.: PCDD, 1982. 75 pp. and appendix.

Wagenaar, A.C.; Douglass, R.L.; Compton, C.P.; and Pettis, L.C. Raising the Legal Drinking Age in Michigan and Maine. Report No. UM-HSRI-81-58. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1981. 367 pp.

Wechsler, H.; Kasey, E.; Thum, D.; and Demone, H. Alcohol level and home accidents. Public Health Reports 84(12):1043-1050, 1969.

Wilson, G.T. Effects of alcohol on human sexual behavior. In: Mello, N.K., ed. Advances in Substance Abuse: Behavioral and Biological Research. Vol. 2. Greenwich, Conn.: JAI Press, 1981. pp. 1-40.

Wingard, D., and Room, R. Alcohol and home, industrial and recreational accidents. In: Aarens, M.; Cameron, T.; Roizen, J.; Roizen, R.; Room, R.; Schneberk, D.; and Wingard, D. Alcohol, Casualties and Crime. Alcohol, Casualties and Crime Project Final Report. Report No. C-18. Berkeley: Social Research Group, University of California, 1977. pp. 39-119.

Wolfgang, M.E. Patterns in Criminal Homicide. Philadelphia: University of Pennsylvania, 1958.

Wolfgang, M. A sociological analysis of criminal homicide. In: Wolfgang, M.E., ed. Studies in Homicide. New York: Harper and Row, 1967, pp. 15-28.

Wolin, S.J.; Bennett, L.A.; Noonan, D.L.; and Teitelbaum, M.S. Disrupted family rituals: A factor in the intergenerational transmission of alcoholism. Journal of Studies on Alcohol 41(3):199-214, 1980.

Wood, L.W. "Lifestyle Management Strategies at New England Telephone." Paper presented at Leadership Strategies-Health Conference, Project Hope, 1980.

Woodside, M. Children of Alcoholics. Albany: New York State Division of Alcoholism and Alcohol Abuse, 1982. 50 pp.

Chapter VII

Treatment: Emerging Trends in Research and Practice

During the past decade, several issues surrounding the treatment of alcoholism have been subject to controversy. Does the unitary disease concept permit reliable diagnosis for the purposes of early detection and treatment planning? Is treatment effective and, if so, can the costs of treatment be contained? Are there distinct subgroups of alcoholic persons? Can treatment efficacy be improved by matching individual patients to specific types of treatment? Should abstinence be the singular goal of treatment or can some problem drinkers engage in nonabusive drinking? If some can, how can these individuals be identified? The issues raised by these questions imply much about the theoretical and practical challenges facing the treatment field.

This chapter will focus on the state of the art of alcoholism treatment, giving special attention to developments not covered in the Fourth Special Report (USDHHS 1981). These developments include innovations in diagnosis, improved procedures for screening and early intervention, new findings on the costs and benefits of treatment, a continuing debate on the use and viability of controlled drinking therapies, and emerging models of treatment efficacy. An encouraging development in recent years has been the enhanced investment in research and clinical training in the alcoholism field, and the concomitant emergence of a multidisciplinary research community actively involved in the problems of treating alcoholism. As the quality and sophistication of clinical research improve, it is likely that many of the unanswered questions will be solved.

Recent Advances in Diagnosis and Nomenclature

Diagnosis, the process of identifying and labeling specific disease conditions, uses precise attributes, or diagnostic criteria, to classify a sick person as having a disease. The importance of diagnostic criteria derives from their usefulness in making clinical decisions, estimating disease prevalence, understanding etiology, and planning treatment. While the diagnosis of alcoholism may seem straightforward to the concerned layperson, it is in fact a complex process.

Limitations in current diagnostic procedures were recently reviewed by McIntosh (1982), who compared data collected in 31 studies of the prevalence of alcohol-related problems in general hospital populations. Variations in the use of diagnostic criteria, as well as lack of conceptual precision in differentiating alcohol dependence from related disabilities, have led to widely differing prevalence estimates of the number of alcoholic patients. In spite of the fact that these patients were in hospitals, most individuals with drinking problems had neither been diagnosed as such nor received appropriate treatment for their alcohol problems.

The traditional unitary disease concept of alcoholism has been challenged by the observation that there may be multiple patterns of dysfunctional alcohol use, which result in multiple kinds of disability. A corollary of the unitary disease concept has been the assumption that alcoholics could be clearly differentiated from nonalcoholics on the basis of their distinctive disease characteristics. Known as the binary classification rule, this assumption has led to the search for universal and singular criteria applicable to all alcoholics. This dichotomous approach has not been particularly helpful to programs interested in early intervention (namely, secondary prevention), nor has it been useful in differentiating prognoses within patient samples in ways that could clarify important questions about treatment efficacy. An alternative approach (Marlatt 1981) characterizes alcohol dependence along a continuum of severity, with no clear demarcation between the beginning of alcoholism and the end of social

drinking. An advantage of this approach is that early detection may be improved when levels of risk have been established.

An important development in the area of diagnosis has been the publication in 1980 of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 1980), better known as DSM-III. As a major revision of the manner in which various disorders, including alcoholism, are diagnosed and classified, DSM-III introduced several innovations designed to address problems in earlier classificatory systems (Spitzer et al. 1980). In contrast to previous editions of DSM, alcoholism is now included within the separate category of substance use disorders rather than as a subcategory of personality disorder. Reflecting a trend toward increased semantic precision, the term "alcohol dependence" is used in preference to the more generic "alcoholism." In addition, a separate category of "alcohol abuse" is added to permit greater differentiation. As delineated in table 1, alcohol dependence is differentiated from alcohol abuse by the presence of tolerance or withdrawal symptoms. Both diagnoses include a pattern of pathological use or impairment in social or occupational functioning due to alcohol. Modeled after diagnostic procedures initially developed for research purposes (Feighner et al. 1972), these criteria provide a systematic, standardized approach to diagnostic decisionmaking.

DSM-III permits evaluation of the individual's condition in terms of five independent dimensions or axes. Axis I describes the major clinical syndromes, including substance use disorders, while Axis II is reserved for concomitant personality disorders. Axis III classifies physical disorders and conditions, a number of which can be coded as alcohol-induced, including alcohol intoxication, alcohol withdrawal, alcohol withdrawal delirium, alcohol hallucinosis, alcohol amnestic disorder, and dementia associated with alcoholism. Axis IV draws attention to the severity of psychosocial stress (e.g., occupational, interpersonal, physical) that may modify the course of the current disorder. Finally, Axis V permits the clinician to indicate the patient's highest level of adaptive functioning during the past year in terms of social relations, occupational functioning, and use of leisure time.

Preliminary evaluations of DSM-III suggest that it provides reliable and valid identification of alcoholics in clinical settings, but that it may be less useful in detecting alcoholics who are not institutionalized (Mulford and Fitzgerald 1981; Helzer et al. 1981; Hesselbrock et al. 1982). Thus, while the DSM-III alcohol-related diagnoses contain many innovative features, the usefulness of this approach for early identification, epidemiological surveys, and treatment planning remains to be evaluated.

The recent development and successful field testing of two standardized interview schedules, the Schedule of Affective Disorders (Weissman et al. 1980) and the Diagnostic Interview Schedule (Helzer et al. 1981), represent a major advance in clinical diagnosis and psychiatric epidemiology. Both schedules provide objective, standardized procedures for diagnosing alcoholism and other clinical syndromes using DSM-III criteria. As these instruments are used with greater frequency to study clinical and population samples, they promise to advance basic knowledge about alcoholism and its relationships to psychiatric syndromes and personality disorders. Data from household surveys using the Diagnostic Interview Schedule in three National Institute of Mental Health Epidemiology Catchment Areas suggest that, at some time during their lives, one in seven adults 18 years of age or older met criteria for alcohol abuse or alcohol dependence.

A related development in the area of alcoholism diagnosis is the international program on diagnosis and classification sponsored jointly by the U.S. Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) and the World Health Organization (WHO 1982). The purpose of this project is to recommend improvements in sections of the International Classification of Diseases (ICD) dealing with alcoholism, drug abuse, and mental health. The first phase was devoted to a systematic examination of concepts and nomenclature pertaining to alcohol and drug abuse (Edwards et al. 1981). Of particular interest to the alcoholism treatment field is the emerging set of concepts, definitions, and criteria that may well provide the basis for the next revision of ICD. Central to the WHO approach to alcoholism is the concept of a dependence syndrome that is distinguished from alcohol-related disabilities (Edwards et al. 1976, 1981). As outlined in table 2, the dependence syndrome is an interrelated cluster of cognitive, behavioral, and physiological symptoms. Alcohol-related disabilities, on the other hand, consist of those physical, psychological, and social dysfunctions that follow directly or indirectly from excessive drinking and dependence.

Table 1. DSM III criteria for alcohol abuse and alcohol dependence

Diagnostic criteria for alcohol abuse	Diagnostic criteria for alcohol dependence
A. Pattern of pathological alcohol use: need for daily use of alcohol for adequate functioning, inability to cut down or stop drinking, repeated efforts to control or reduce excess drinking by "going on the wagon" (periods of temporary abstinence) or restricting drinking to certain times of the day, binges (remaining intoxicated throughout the day for at least 2 days), occasional consumption of a fifth of spirits (or its equivalent in wine or beer), amnesic periods for events occurring while intoxicated (blackouts), continuation of drinking despite a serious physical disorder that the individual knows is exacerbated by alcohol use, drinking of nonbeverage alcohol.	A. Pattern of pathological alcohol use: need for daily use of alcohol for adequate functioning, inability to cut down or stop drinking, repeated efforts to control or reduce excess drinking by "going on the wagon" (periods of temporary abstinence) or restricting drinking to certain times of the day, binges (remaining intoxicated throughout the day for at least 2 days), occasional consumption of a fifth of spirits (or its equivalent in wine or beer), amnesic periods for events occurring while intoxicated (blackouts), continuation of drinking despite a serious physical disorder that the individual knows is exacerbated by alcohol use, drinking of nonbeverage alcohol.
B. Impairment in social or occupational functioning due to alcohol use: violence while intoxicated, absence from work, loss of job, legal difficulties (e.g., arrest for intoxicated behavior, traffic accidents while intoxicated), arguments or difficulties with family or friends because of excessive alcohol use.	B. Impairment in social or occupational functioning due to alcohol use: violence while intoxicated, absence from work, loss of job, legal difficulties (e.g., arrest for intoxicated behavior, traffic accidents while intoxicated), arguments or difficulties with family or friends because of excessive alcohol use.
	Either tolerance or withdrawal:
C. Duration of disturbance of at least 1 month.	C. Tolerance: need for markedly increased amounts of alcohol to achieve the desired effect, or markedly diminished effect with regular use of the same amount.
	D. Withdrawal: development of alcohol withdrawal (e.g., morning "shakes" and malaise relieved by drinking) after cessation of or reduction in drinking.

Source: American Psychiatric Association 1980.

According to the WHO dependence model, a complete description of an individual's alcohol-related pathology must include statements concerning the nature and severity of dependence, the kinds and degrees of disability, and the personal and environmental factors that influence the drinking problem. The WHO model departs significantly from DSM-III and the older binary classification schemes by emphasizing that both dependence and alcohol-related disabilities exist in degrees rather than in an all-or-none state.

In the brief period since it was first introduced, the dependence syndrome construct has received considerable attention from researchers and clinicians. A number of instruments have been developed to assess its usefulness (Stockwell et al. 1979; Skinner and

Table 2. Constituent elements of the alcohol dependence syndrome

Elements	Interpretation/examples
Narrowing of the drinking repertoire	The drinking pattern tends to become stereotyped around a regular schedule of almost continuous daily consumption.
Salience of drink-seeking behavior	Drinking is given higher priority than other activities in spite of its negative consequences.
Increased tolerance to alcohol	More and more alcohol is required to produce behavioral, subjective, and metabolic changes; large amounts of alcohol can be tolerated.
Repeated withdrawal symptoms	Tremulousness, sweatiness, nausea, etc., appear after short periods of abstinence.
Relief drinking	Withdrawal symptoms are relieved or avoided by further drinking, especially in the morning.
Compulsion to drink	Subjective awareness of craving for alcohol exists, as well as impaired control over quantity and frequency of intake.
Readdiction liability	The syndrome tends to be rapidly reinstated when drinking is recommenced after a period of abstinence.

Source: Adapted from Edwards et al. 1976, 1981.

Allen 1982; Hesselbrock et al. 1983). Research in both experimental and clinical settings suggests that the severity of dependence can correlate positively with attendance at a treatment clinic (Skinner and Allen 1982), cravings for alcohol after a "priming" drink (Kaplan et al. 1983), and failure to control drinking following relapse (Orford et al. 1976; Polich et al. 1981). While further research is needed, the dependence syndrome construct shows considerable promise for early detection, diagnosis, and treatment planning.

Differential Assessment

Both DSM-III and the WHO dependence model represent a general movement toward differential assessment as evidenced by the use of multiple criteria to provide a comprehensive evaluation for treatment planning. Ideally, specificity of diagnosis should lead to specificity of treatment, an important goal in the delivery of treatment services for three essential reasons: (1) economy of cost, (2) avoidance of inappropriate or ineffective treatment, and (3) increased efficacy. Surprisingly, outside the area of personality assessment, little interest has existed until recently in differential assessment of the alcoholic person. This is due in part to assumptions about the unitary nature of alcoholism, and in part to the limited methods available to evaluate alcoholics.

Recent advances in evaluation methodology (Meyer et al. 1981) have stimulated research in this area, and a number of assessment procedures have been developed. In addition to those already discussed, several investigators (Skinner and Allen 1982) have demonstrated the usefulness of assessing drinking patterns and alcohol-related problems in an effort to identify individual differences related to

treatment outcome. Other instruments have been developed recently to provide differential assessment of stages of alcoholism (Mulford 1980), client liabilities associated with poor treatment response (Costello and Baillargeon 1981), severity of addiction-related problems (McLellan et al. 1980), and stability of the male alcoholic's marital situation (O'Farrell et al. 1981). With the burgeoning application of computer technology to individual testing and statistical data analyses, the benefits of differential assessment may well become routine in clinical settings.

Screening and Early Detection of Alcoholism

Consonant with recent conceptual developments in the diagnosis of alcoholism, there has been increasing interest in the development of a simple and accurate screening procedure that could facilitate early identification of alcohol dependence. Clearly, early casefinding can improve the effectiveness of treatment and reduce its costs. Research on early identification has progressed on two relatively independent planes: (1) the search for biochemical markers for alcoholism and (2) the elucidation of psychosocial indicators.

Biochemical Markers

The accumulation of research findings, some of which have already been noted in previous chapters of this report, suggests that several laboratory tests may be useful in the early detection of alcohol abuse. Serum gamma-glutamyl transpeptidase (GGTP) has been suggested as an indicator of heavy alcohol consumption among problem drinkers (Reyes and Miller 1980). Although its usefulness may be affected by concurrent liver pathology, drug use, and individual differences among heavy drinkers (Garvin et al. 1981), its discriminative ability is enhanced considerably when interpreted in conjunction with mean corpuscular volume (MCV) and other tests (Mayfield and Johnston 1980; Chick et al. 1981). That routine blood chemistries may be a useful adjunct for detecting alcoholism is suggested by the results of several studies (Ryback et al. 1980, 1982) that have found that the profiles of 25 biochemical tests differentiated between known alcoholics and nonalcoholics with a high degree of accuracy.

Psychosocial, Clinical, and Combined Assessments

Because some psychosocial symptoms (e.g., escape drinking, concern about a drinking problem, alcohol-related accidents) may appear relatively early in the alcoholic's drinking career, their assessment by means of interviews or self-administered questionnaires has received increasing attention by researchers interested in screening and early diagnosis (Skinner et al. 1981).

Clearly, the most investigated self-administered diagnostic instrument continues to be the Michigan Alcoholism Screening Test (MAST). Consisting of 25 true/false statements describing the typical medical, social, and behavioral problems associated with excessive drinking, the MAST has demonstrated a considerable degree of validity in distinguishing between known groups of male alcoholics and male nonalcoholics (Brady et al. 1982). Concurrent with validation of the MAST has been the development of a variety of similar screening instruments (Brown and Lyons 1981; Skinner et al. 1981). These tests are rapid, inexpensive, and relatively accurate when used under proper conditions. Their simplicity, or gender specificity, however, may limit their usefulness for general population screening, particularly as the obvious intent of the questions leaves them vulnerable to deliberate falsification or unconscious denial.

Recognizing that psychosocial tests have limitations when used in isolation, investigators have begun to use clinical, laboratory, and psychosocial tests in combination. The results of one study (Skinner et al. 1980) underscore the advantages of this approach. Using the Munich Alcoholism Test, a new instrument that combines clinical signs and symptoms (as identified by the physician) with self-report information provided by the patient, it was found that the two types of indicators occurred with relative independence of each other. Psychosocial problems predominated in the younger patients, while clinical signs and symptoms were more frequent in the older drinkers.

From Screening to Early Intervention

Developments in several countries indicate that concerted efforts are now underway to link new screening technologies to low-cost early intervention strategies. Building on previous research (Edwards et al. 1977), which

suggested that one session of advice can be as effective as conventional treatment for some alcoholics, a pilot program is currently being evaluated in Scotland to determine the effectiveness of a brief intervention with problem drinkers identified in a general hospital setting (Chick et al. 1982). Preliminary results of a 1-year followup indicate that a single 35-minute counseling session may reduce drinking and its consequences in a significant proportion of newly identified problem drinkers.

In Sweden, an early intervention program was conducted with middle-aged heavy drinkers identified by means of elevated GGTP values (Kristenson 1982). Individuals randomly assigned to a control group received advice to limit their alcohol consumption. Those assigned to an intervention group were repeatedly encouraged to drink less and, in addition, received feedback about their GGTP levels. Compared with the controls, the intervention group showed significant reductions in absenteeism, hospitalizations, and mortality up to 6 years after the initial screening.

In France, screening for problem drinking and alcohol dependence is conducted routinely in industry, health care settings, and the courts. Individuals identified by means of a simple clinical exam (the Le Go grid method) and biochemical tests (GGTP and MCV) are referred to a nationwide system of more than 130 early intervention clinics. While the effectiveness of these clinics has not been studied systematically, the program demonstrates that, from a public health perspective (Babor et al. 1983), early intervention in a large population is now feasible.

Job-Based Interventions

The process by which problem-drinking employees within a work organization are identified and engaged in treatment has been the subject of much discussion (Googins and Kurtz 1980; Roman 1982). Initially, it was advocated that supervisors and managers be trained to identify impaired job performance, and then to confront the employee to determine the necessary corrective action. Supervisors have been found to be inconsistent in confronting their problem-drinking employees (Kurtz et al. 1980), depending on their own attitudes about alcohol use and abuse and their perceptions of the union's support for the program (Beyer et al. 1980). With the impressive expansion of job-based employee assistance programs during the past decade, there has been a shift in emphasis away from the sole identification of alcohol problems to include any employee problem that adversely affects performance (Roman 1981). In the more recently developed employee assistance programs, the role of supervisor as diagnostician has been deemphasized in favor of the more traditional roles of supervising performance and focusing on unacceptable changes in performance as the basis for intervention and referral.

One recent study investigated how the threat of disciplinary action affects treatment outcome (Freedberg and Johnston 1980). Men who chose to enter treatment as an alternative to disciplinary action were compared with others who sought treatment voluntarily. Both groups were similar with respect to job functioning and drinking behavior after 1 year, a finding that denotes the disciplinary process as a useful way to engage employees in treatment. Moberg et al. (1982) report followup data on several hundred inpatients from an abstinence-oriented industrial program. Forty-six percent were abstinent 3 months after treatment, while 37 percent were abstinent after 9 months. About 20 percent were drinking moderately at each followup, but those listed as moderate drinkers at 3 months had a high relapse rate 9 months after treatment. Although social support and employer involvement had a positive influence on outcome, type of referral (voluntary vs. coercive) made little difference.

Despite increasing interest in the evaluation of occupational programs, the relative lack of studies in this area, together with limited access to the worksite, have made it difficult to assess the overall contribution of these programs to improved job performance and reduced health care costs.

Alcoholism Treatment: Programs and Therapeutic Approaches

The treatment system that emerged following the Second World War is varied, complex, and still in the process of development. Many of its programmatic components (e.g., detoxification facilities, inpatient hospital and residential programs, halfway houses, and outpatient clinics), and the therapeutic approaches employed in these components, have only recently begun to receive systematic research attention. What is the most appropriate setting for treatment? What are the most efficacious therapeutic approaches? What is the

optimal reimbursement policy for medicare, medicaid, and private insurance carriers?

Detoxification

The management of acute alcohol intoxication and the concomitant alcohol withdrawal syndrome is commonly referred to as detoxification. In the late 1960s, specialized detoxification facilities were developed to address the needs of the public inebriate; these facilities expanded rapidly following widespread adoption by the States of the 1974 Uniform Alcoholism and Intoxication Treatment Act decriminalizing public intoxication. At first these facilities were closely associated with hospital emergency services, but in recent years several alternatives to hospital-based detoxification have emerged. A recent survey of State Alcoholism Authorities (Den Hartog 1982) indicated a threefold increase in the number of States operating or purchasing nonhospital-based detoxification since 1975. The most controversial of these alternatives has been "social setting" detoxification, in which the use of drugs such as diazepam and chlordiazepoxide is avoided in the management of withdrawal in favor of a supportive social climate designed to engage the patient in further treatment.

Because the different detoxification methods have not been assessed directly in controlled comparisons, little is known about the relative merits of various approaches in relieving the distress associated with alcohol withdrawal, preventing the risks of medical complications, and facilitating the process of referral to long-term treatment. The need for hospital-based, medical detoxification, as well as the referral to social setting facilities, depends on the patient's physical condition, nutritional status, severity of alcohol dependence, and overall medical evaluation.

The growth of social setting detoxification has resulted from its lower cost, the changing attitudes about the use of sedatives and tranquilizers in withdrawal management, and evidence indicating that a significant number of patients do not experience serious medical complications during withdrawal (Diesenhaus 1982). A recent review of the published literature in the United States, Canada, and Europe (Den Hartog 1982) concluded that detoxification could occur humanely, safely, and efficiently in nonhospital settings. These reports need to be substantiated by systematic research, since it is not clear what proportion of alcoholics require detoxification in hospital settings. Moreover, while the proponents of social setting detoxification contend that it will facilitate referrals to long-term treatment, insufficient evidence exists to conclude that this type of referral will occur more efficiently in either social or medical settings.

What is clear from the experience of nonhospital detoxification programs is that medically oriented inpatient detoxification may not be necessary for the majority of referrals who are not severely dependent and who are otherwise in good health (Diesenhaus 1982). With the increasing availability of ambulatory and inpatient social setting detoxification, careful study of the nature and role of detoxification in the rehabilitation process would seem warranted. The long-range implications of this trend need to be considered.

The high rate of relapse among detoxified patients is another major concern to service providers. Although it may be unrealistic to expect an initial care component to accomplish much more than detoxification and referral, at present a small proportion of the public inebriate population utilizes a disproportionate share of detoxification resources. Further, these patients often refuse recommended referrals to intermediate care facilities. One study of a predominantly skid row population (Fagan and Mauss 1978) found that fewer than one-third accepted their recommended treatment referral after detoxification. Another study (Richman and Smart 1981) found that the probability of further referral was lowest in those patients having a history of multiple detoxifications. Two possible solutions to the problem of "resource absorption" by detoxification repeaters have been suggested. The first is the greater availability of comprehensive services to the skid row population; the second is the use of legal coercion to motivate the public inebriate to enter and remain in treatment (Fagan and Mauss 1978).

Benefits of Treatment

The rapid growth of insurance coverage for alcoholism treatment has been predicated in part on the assumption that such treatment is cost-beneficial, i.e., the long-term costs to both the individual and society will be reduced. Alcoholics and their families have been found to use a disproportionate amount of inpatient and outpatient medical services for a wide variety of physical problems related to excessive drinking (Roghmann et al. 1981; Putnam 1982a). Reflecting an increased concern with the implications of treatment re-

imbursement policy, a number of new studies have used the improved methods of cost-effectiveness and cost-benefit analysis to show that cost savings can be accrued over a period of time (Swint and Nelson 1977). The first major review of research conducted during the 1970s (Jones and Vischi 1979) found surprising consistency across 12 studies. Despite some methodological problems, these studies indicated significant reductions in medical care use and expenditures related to various kinds of alcoholism treatment, amounting to a 40-percent median reduction in sick days and accident benefits. Additional studies since that time have confirmed this conclusion (Saxe et al. 1983).

Substantiating these findings is a recently conducted study of State employees of California in which 90 families with an alcoholic member, all enrolled in Blue Cross/Blue Shield, were followed for a period of 5 years. Results indicated that the total medical care costs per family member decreased substantially over time once the alcoholic member entered treatment (Holder and Hallan 1981).

These studies have been conducted predominantly within health maintenance organizations (HMOs), primarily because alcoholics are relatively easy to track within these comprehensive health programs. A major study of alcoholism treatment in HMOs recently completed by the Group Health Association of America (Plotnick et al. 1982) compared the utilization of four HMO outpatient alcoholic treatment programs by alcoholic persons from 2 years before entering treatment to 48 months after treatment. The study revealed significant reductions in general health care use for the alcoholic persons and their family members. In another HMO study (Forsythe et al. 1982), treated alcoholics were compared with nonalcoholics over a 4-year period. Although the cost differential between the two groups was substantial during the entire study periods, there was a significant decline in alcoholics' demand for services following referral to treatment.

Focusing on the illnesses that may precipitate alcoholics' referral to treatment, Putnam (1982a) found that alcoholics manifested a high number of physical and emotional illnesses. Problems most likely to be associated with the alcoholics' hospitalizations entailed psychosocial difficulties such as anxiety, depression, and marital discord, as well as accidents, drug overdoses, and violence. In many cases, the alcoholics were found to be seeking inappropriate care and receiving inappropriate treatment, since the alcoholism underlying their illness was often not properly diagnosed.

In a related study of the same HMO (Putnam 1982b), alcoholics who received outpatient alcoholism treatment were compared with alcoholics who were identified but refused to accept treatment. An examination of the utilization rates for medical care services before and after referral to treatment revealed that both groups showed a higher level of service use in the 4-month period prior to referral. Those who accepted alcoholism treatment, however, showed a progressive decrease in use of services during the subsequent period, while those who refused treatment increased their demand for services approximately 15 months after the attempted referral. This increase is related to a high incidence of problems associated with accidents, drug overdoses, and violence, and highlights the importance of appropriate diagnosis and treatment to reduce both the human and the social costs of alcoholism.

Finally, a significant non-HMO-based study (Holder and Hallan 1981) followed the families of 90 State employees in California for a period of 5 years. Each family had an alcoholic member and all were enrolled in Blue Cross/Blue Shield. The study indicated that total medical care costs per family member decreased substantially over time once the alcoholic family member entered treatment. At the end of the study, inpatient costs per person per month of both the comparison families (N=83) and the alcoholic families (N=90) were similar, and outpatient costs of the comparison families were actually higher.

Although many of the studies of alcoholics' use of health services are limited in scope, methodology, and populations investigated, the evidence suggests that: (1) alcoholics and their families initially use more health care services than nonalcoholics; (2) this elevated demand can be reduced substantially by treatment for alcoholism; and (3) the benefits of alcoholism treatment clearly outweigh its costs.

Treatment Settings

Studies comparing the effectiveness of inpatient programs with outpatient and day hospital treatment are important because of the potential for improved cost-effectiveness and the appeal these approaches may have for alcoholics who reject inpatient or residential care. In one study (Longabaugh et al. in press), patients participating in a day hospital pro-

gram (while returning home at night) were given the same behavioral treatment program that hospitalized inpatients were receiving. At 6-month followup, both groups were comparable on measures of drinking behavior, need for rehospitalizations, and social and occupational functioning. The partial hospitalization group was superior on measures of psychological well-being. Given the lesser cost of partial hospitalization, the authors conclude that this form of treatment is more cost-effective. In another study, comparable findings are reported after 1-year followup of 100 patients who were randomly assigned either to a day clinic or to an inpatient facility offering a similar treatment program (McLachlan and Stein 1982). These results support the conclusion that the two types of treatment setting may be equally effective.

Studies comparing the results of inpatient and outpatient programs have generally not shown significant differences in the effects of treatment setting (see review by Cole et al. 1981). However, it seems likely that day hospital and outpatient treatment programs will prove to be substantially less effective for certain groups of patients, and Spicer et al. (1981) caution that conclusions regarding equal effectiveness should be limited to clients who are appropriate for each type of program. Many studies comparing outpatient with inpatient treatment have not controlled for the possibility that patients choosing outpatient settings are less severely dependent. Inpatient treatment seems indicated when motivation is weak to continue treatment, when patients are psychotic, depressed, or suicidal, and when complicating physical disabilities are present. Other factors which may also influence the choice of treatment setting include patients' social stability and the number and severity of their symptoms, as well as the ability of programs to respond to individual needs (Cole et al. 1981; Spicer et al. 1981). Research is needed to identify the characteristics of patients most likely to benefit from an outpatient program, followed by treatment-matching studies to test the validity of the identified patient types. An additional obstacle to the substitution of residential treatment by outpatient treatment is the high rate of client attrition usually encountered in the outpatient setting.

Matching Clients with Programs

Considerable selection takes place on the part of both the client and the referral agent in the natural process of identifying alcoholics and referring them to treatment (Pattison and Kaufman 1981; Beckman and Kocel 1982). Despite the increasing variety of programs, settings, and treatment modalities, many alcoholics do not have the opportunity to find an informal match between their own specific needs and the type of treatment available. This is particularly true of special needs populations, such as women, ethnic minorities, the multidisabled, the elderly, and skid row alcoholics. For these groups, access to treatment and successful rehabilitation are often impeded by cultural barriers, financial constraints, and program design characteristics. Since considerable attention has already been given to the needs of these groups in the Fourth Special Report (USDHHS 1981) and other sources (Diesenhaus 1982; NIAAA 1982), this section will provide a brief update on the issues common to all special needs populations.

Because middle-aged white men represent the typical clientele of most treatment facilities, programs often are not designed with the needs of other groups in mind. These groups may thus be reluctant to seek help because of a number of structural and group-specific barriers that restrict access to appropriate facilities. For example, a survey of 53 California treatment facilities (Beckman and Kocel 1982) suggested that women alcoholics were less likely to enter programs lacking child care services, professional staff, and aftercare programs. However, Institute experience in providing services for women reveals that many women do not utilize child care services even when provided. Other barriers to treatment for some groups are language differences and composition of treatment staff. Minority staff members represent only a small proportion of the Nation's alcoholism treatment personnel (NIAAA 1980). Yet another barrier may be financial constraints. Women and minorities tend to be overrepresented in publicly funded facilities and underrepresented in private ones (NIAAA 1980). Without programs' sensitivity to the needs of these populations, many individuals may fail to seek treatment until their alcoholism has reached a severe stage of development.

With the growing recognition that utilization rates may be improved by removing barriers to access, greater attention is now being given to special population groups in the design of treatment programs. Some facilities seeking to attract Hispanic and Native American clients are using folk medicine and native healing approaches as alternatives or adjuncts

to traditional medical and psychiatric treatments. Counselors and other treatment staff members are being matched to the sex and ethnic background of their clients. Also, conveniently located, community-based programs, at times staffed and planned in collaboration with special population groups, are appearing more frequently (NIAAA 1982).

What is uncertain, at this time, is the impact the ADM block grant program will have on treatment programs. Of particular interest will be the differential rates of service use across States, by both the general population and special population groups. As these programs become available to special population groups, research will need to move from program descriptions to actual evaluation studies in which programs designed for special population groups are compared with more traditional approaches.

One exception to the trend to develop services for special population groups and subtypes of alcoholic persons has been the small number of combined programs serving both alcoholics and drug dependent persons. Although combined treatment for alcoholics and drug abusers has not been widely adopted, the feasibility of such programs may have important implications for the planning of future treatment services, given the increased tendency for patients to present multiple abuse or addiction patterns at the time of treatment (Sokolow et al. 1981).

Therapeutic Approaches

Several diverse treatments are often delivered within the context of alcoholism services, depending on the resources and needs of clients, as well as the specific training or orientation of the staff. In many cases, a combination of therapeutic interventions is provided to all clients, under the assumption that multiple treatments stand a good chance of meeting at least some of each client's needs. As the alcoholism treatment system has grown in size and complexity, evaluating individual therapeutic approaches in isolation from one another has become more difficult. Many studies reported in the literature involve adding a treatment of interest to a facility's standard therapeutic program, or are descriptive evaluations rather than clinical trials comparing one or several treatments with the absence of treatment. Studies discussed here generally employed an experimental methodology, as firm conclusions about efficacy can be made only through systematic comparisons.

Behavior Therapy

Behavioral elements most frequently applied in treatment programs include social skills and assertiveness training, contingency management, deep muscle relaxation, self-control training, and cognitive restructuring (Miller and Mastria 1977). Despite their widespread adoption, these methods have not been subject to systematic evaluation with random assignment of large numbers of patients to various treatment conditions.

Aversion therapy.--This approach to treatment grew from Pavlovian conditioning theory, which predicts that the sight, smell, and taste of alcohol will acquire aversive properties if repeatedly paired with noxious stimuli. A thorough review of the research in this area (Miller and Hester 1980) concluded that emetic (nausea producing) aversive conditioning can be effective for employed, married, well-motivated alcoholics, but that the effectiveness of electrical aversion is doubtful. These conclusions are supported by recent work (Cannon et al. 1981) comparing these two aversion procedures when used in addition to a standard treatment program. Patients exposed to emetic conditioning exhibited significantly greater improvement after 6 months than patients exposed to conditioning with electric shock, but the advantage after 1 year was not significant.

Work has also proceeded on covert sensitization, a procedure in which imagined scenes of alcohol ingestion are paired with nausea induced by verbal suggestion. This method may overcome some of the practical disadvantages of emetically based aversion therapy. Some recent studies have offered support for this procedure. One study found that patients receiving covert sensitization remained abstinent longer and demonstrated better psychosocial adjustment than patients in control groups (Elkins 1980). In a related study, patients receiving covert sensitization in a standard inpatient treatment program showed greater improvement over a 4-year period than patients who received insight-oriented therapy (Olson et al. 1981).

Extinction.--Recent experiments have shown that alcohol-related stimuli (such as the sight or smell of an alcoholic beverage) can induce both physiological changes and altered behavior in alcoholic patients (Kaplan et al. 1983; Pomerleau et al. 1983). Because condi-

tioning processes related to alcohol craving and tolerance development may affect the rapidity of relapse after a period of abstinence, some have proposed that conditioned extinction be made an essential part of treatment (Hinson and Siegel 1980). Extinction of the effectiveness of alcohol-related cues is achieved by repeatedly presenting them unaccompanied by either alcohol ingestion or intoxication. This may theoretically weaken the link between these stimuli and drinking behavior, with a consequent improvement in treatment outcome. To date, a few successful case studies have been reported (e.g., Blakey and Baker 1980). Additional systematic investigation should clarify these data from clinical research studies.

Coping skills training.--Behavior therapists have recognized the importance of teaching new, adaptive coping skills to patients who engage in dysfunctional behaviors. These skills include altering conditions before or after drinking, as well as developing alternative ways of coping with persons, events, and feelings that may have served to maintain abusive drinking (Miller and Mastria 1977). A number of studies have demonstrated the benefits of teaching social and other coping skills (e.g., Ferrell and Galassi 1981; Oei and Jackson 1980, 1982), although others have not confirmed these findings (c.f., Sanchez-Craig and Walker 1982). Chaney et al. (1978) have tested a cognitive-behavioral model of treatment, characterized as "relapse prevention" because of its focus on identifying highrisk situations. Patients given skills training had less severe (though no less frequent) relapse episodes, were more likely to be employed, and attended aftercare more regularly than patients in control groups. A replication with alcoholic persons of higher socioeconomic status than the population originally studied found both skill training and discussion groups to be superior to a minimal-treatment group, but not different from each other (Jones et al. 1982). Further study should capitalize on the increasingly widespread use of these methods.

Selecting Treatment Goals

Interest in therapies with alternative drinking goals was sparked in part by findings that a small proportion of treated alcoholics reportedly were able to return to moderate drinking without serious problems (Pattison 1976). The Rand study (Armor et al. 1978), for example, reported that some "definitely alcoholic" persons were capable of drinking moderately 6 months after treatment and of maintaining moderation up to 12 months later. More recently, Moos, Finney, and Chan (1981) found that 12 months after abstinence-oriented treatment, 25 percent of the recovered patients were drinking in moderation. It should be noted that the term moderation in these studies refers to an average consumption of less than 3 ounces of absolute alcohol per day, in the absence of alcohol-related symptoms, work problems, or rehospitalizations.

Several explanations for these findings seem to be emerging from studies employing longer followup intervals and more refined assessments of patient characteristics. The second part of the Rand study (Polich et al. 1981) revealed that the relapse rate 4 years after treatment was higher (41 percent) among those who had been drinking moderately at 18 months than among those who had been abstinent at that time (30-percent relapse rate). Other research (Orford et al. 1976; Finney and Moos 1981), as well as the Rand studies, suggests that those individuals characterized as moderate drinkers at followup tend to have had less severe alcohol dependence and fewer drinking problems prior to treatment. A 2-year followup of patients receiving abstinence-oriented treatment (Finney and Moos 1981) compared persons drinking moderately at 6 months following treatment with persons who abstained. Those who returned to moderate drinking soon after treatment were more likely to relapse to heavy drinking than those who remained abstinent for 6 months and who then attempted moderate drinking. Thus, while moderate drinking seems possible for some patients following treatment, this phenomenon may be explained by the highly variable course of alcoholism over time (some alcoholics take longer to relapse than others), and by the existence of individual differences among patients in severity of alcohol dependence, social supports for moderate drinking, and a variety of other mitigating factors.

Another possible explanation lies in the nonstandard interpretation of the term alcoholic. In many studies that report moderate drinking by alcoholics, little information has been provided about the patients' severity of dependence, history of alcohol abuse, or extent of alcohol-related disability. In studies reporting such data, moderate drinking patients tend to be less "alcoholic" at the time they enter treatment. Had stringent criteria for alcohol dependence been applied, it is conceivable that the drinking problems of many of these patients would be classified as

alcohol abuse rather than alcoholism. Similar semantic problems cloud the meaning of moderation. Several studies (Armor et al. 1978; Moos et al. 1981) have included amounts of up to 5 ounces of absolute alcohol per day within their definitions of moderate drinking. While many patients were drinking far below this limit, the use of such a high cutoff point would tend to inflate estimates of the proportion of moderate drinkers. Furthermore, to the extent that cognitive impairment and other alcohol-related disabilities may result from consuming these amounts (Wilkinson and Sanchez-Craig 1981), this liberal definition of moderation may be questioned in terms of its health implications.

The controversies generated by such studies as the Rand reports (Armor et al. 1978; Polich et al. 1981) illustrate the need to apply sophisticated and systematic research methodology to explorations of the following questions: In the small number of alcoholic subjects who have reportedly established a pattern of moderate drinking, how stable is that pattern over time? How much is this drinking pattern altered by stress, anxiety reactions, and environmental factors, such as media advertising and the cost of alcoholic beverages? What are the risks of resuming drinking compared with abstinence in this group? What are the characteristics of patients who have developed moderate drinking patterns in terms of age, sex, socioeconomic level, marital status, and drinking history? To what extent does the existence of a belief in moderate drinking increase the risk of relapse in alcoholic patients?

Despite questions raised about treatment goals for alcoholic persons, research has nevertheless proceeded on the effects of teaching moderation to socially stable problem drinkers (Heather and Robertson 1981). Pomerleau et al. (1978) have demonstrated that behavioral treatment can be used effectively for teaching moderation to middle-income nonalcoholic problem drinkers, while others have explored some dimensions of teaching nonproblem alcohol consumption skills. Effective elements of treatment that have been identified include modeling and repeated practice of a clearly delineated pattern of moderation (Strickler et al. 1981), and empathy on the part of therapists (Miller et al. 1980). These must be viewed as suggestive findings, since the results of these treatment studies have yet to be confirmed with various subgroups of problem drinkers, in natural environment settings, or with studies of long-term outcomes.

In summary, the issues surrounding moderate, nonproblem drinking as a viable treatment option for nonalcoholic problem drinkers are not likely to be completely resolved until progress has been made in those areas most relevant to this controversy: improved nomenclature, more precise diagnostic criteria, new techniques for differential assessment, earlier treatment interventions, better matching of client needs to specific treatments, and improved research methodologies. It should be clear that while continued exploration and assessment of a variety of treatment options and goals for nonalcoholic and/or prealcoholic persons are appropriate endeavors, the consensus of clinical opinion is that the most appropriate goal for alcoholic persons is abstinence.

Alcoholics Anonymous

With nearly 50 years of service to alcoholic persons and their families, the fellowship of Alcoholics Anonymous (AA) has not been the subject of systematic research to study its long-term and short-term efficacy. To this end, Glaser and Ogborne (1982) reviewed the clinical and research literature, and have proposed a number of research questions and designs to highlight the most effective elements of the AA program and describe those persons for whom AA participation is the preferred approach.

Efforts to identify patients who are best suited to the AA approach have thus far sought to identify characteristics of those who have become actively involved in the AA program (e.g., Boscarino 1980; O'Leary et al. 1980). Some common characteristics have been identified, including need for structure and for affiliation with a group. As yet, no consistent profile has emerged to characterize successful AA members in terms of degree of impairment, social stability, or emotional disruption. This state of affairs has been attributed to inconsistencies of findings among studies, differing focuses of attention across studies, and methodological inadequacies (Ogborne and Glaser 1981).

Alcoholics Anonymous is a major voluntary resource in the treatment of alcoholism, with a reported membership of 476,000 in the United States and Canada in 1980. The most comprehensive information on membership comes from the organization itself (Alcoholics Anonymous 1981). The triennial sample sur-

veys conducted since 1968 profile characteristics and trends of the membership. For example, membership has increased from 170,000 in 1968 to 476,000 in 1980; the proportion of women increased from 22 percent in 1968 to 31 percent in 1980; the proportion of people 30 and under has increased to 14.7 percent in 1980 from 11.3 percent in 1977 when this trend toward younger membership was first noted; and the proportion who state counseling agencies and treatment facilities as important in their attending their first AA meeting increased from 19 percent in 1977 to 26 percent in 1980. (Of those members beginning AA since the 1977 survey, 33 percent indicate counseling and treatment referrals were most responsible for first attendance.)

Dynamic Psychotherapy and Group Therapy

Numerous descriptions of the application of dynamic psychotherapy to the treatment of alcoholism exist (Bean and Zinberg 1981; Zimberg 1982), but almost no outcome studies evaluating this approach to treatment have been conducted. In recent years, psychotherapeutic approaches have given way to, or have been combined with, behaviorally oriented treatment in many settings. Some clinicians have argued against the use of psychotherapy on the grounds that it may strip patients of defense mechanisms that could be used in the service of sobriety (Wallace 1978), and that it makes demands that alcoholics are unready to meet in the early phases of recovery (Vaillant 1981). Nevertheless, there are indications that psychodynamically oriented group psychotherapy may in fact be preferred for certain subgroups of alcoholic persons (Kissin 1977).

A considerable body of literature describes group therapy techniques in the treatment of alcoholism (e.g., Vannicelli 1982), but with only a few evaluative studies to support its efficacy. A recent study by Oei and Jackson (1980) compared group with individual therapy, each of these approaches being used to provide social skills training to some patients and traditional supportive therapy to others. Significant improvement was found only in patients given social skills training, with greater improvement in those trained in a group setting than among those treated individually. Given the potential cost-effectiveness of group therapy, as well as its widespread use, these findings should be followed up with comprehensive evaluative studies.

Family Treatment

The accumulating evidence documenting the deleterious effects of alcoholism on families has prompted heightened interest in family treatment of alcoholism, as described in some detail in the Fourth Special Report (USDHHS 1981). Although the therapeutic value of family treatment is well documented and heralded for many related problem behaviors (Stanton and Todd 1982), its unique contribution and efficacy with alcoholism treatment remain to be fully demonstrated and evaluated (Steinglass 1979; Pattison and Kaufman 1981). Preliminary results from a study comparing degrees of spouse involvement in outpatient alcoholism treatment indicate certain advantages for marital therapy, but 18-month outcome data have not yet been reported (McCrady and Noel 1982). Considerable work in evaluating family therapy with alcoholic families is needed, especially efforts to match specific treatments to the problems presented by different families.

Pharmacotherapy

The value of pharmacological agents such as disulfiram (Antabuse) as a deterrent to drinking and various patient factors associated with favorable outcome is of continuing research interest. In recent work, Fuller and Roth (1979) randomly assigned 128 men to receive either a standard dose of disulfiram, a pharmacologically inactive dose, or a daily dose of the vitamin riboflavin. The standard dose of disulfiram was more effective than riboflavin in producing abstinence after 1 year, although differences were small (Fuller and Williford 1980).

One aspect of treatment with disulfiram has been patient noncompliance, that is, the patient's unwillingness to continue regular ingestion. Azrin et al. (1982) studied compliance-enhancement procedures with patients in a rural outpatient clinic. A behavioral "disulfiram assurance" program, involving five sessions of stimulus control training, role playing, and communication skills training, was highly effective in promoting abstinence in married clients, but had little effect on single clients. However, the addition of behavior therapy (training in drink refusal, social skills, and muscle relaxation, and counseling in recrea-

tion activities and job-finding) was sufficient to produce nearly complete abstinence for single clients. These are intriguing results, especially since they were obtained in relatively few sessions and with only monthly followup contacts thereafter.

Anotner study tested the effects of a compliance-enhancement procedure in an industrial setting (Robichaud et al. 1979) and demonstrated the effectiveness of closely supervised ingestion of disulfiram for reducing absenteeism, but only during the treatment period. The findings regarding disulfiram should be regarded as preliminary, but they do suggest that disulfiram may have a useful role in treatment if compliance can be ensured. Future studies of compliance with broader ranges of clients are needed and may be facilitated by newly developed methods for monitoring use of disulfiram (e.g., Paulson et al. 1977; Neiderhiser and Fuller 1982).

A possible role for lithium in the treatment of alcoholism has been considered because of its effectiveness in treating affective disorders and the relatively high incidence of these disorders in alcoholics. The findings thus far have been equivocal. In one study, depressed patients taking lithium had fewer drinking episodes compared with placebo control patients, but without any greater alleviation of the depression than occurred in the control patients (Kline et al. 1974). In other studies, however, depressed patients did not consume less alcohol during lithium therapy (Pond et al. 1981). The possible value of lithium in treating alcoholics thus remains uncertain, with more definitive studies required, employing double-blind procedures and comparisons with other forms of treatment (McMillan 1981).

Ciraulo and Jaffe (1981) have reviewed the use of tricyclic antidepressants in alcoholics and report success in treating initial symptoms of withdrawal, such as anxiety, depression, and somatic discomfort, only within the first 2 to 3 weeks after cessation of drinking. In a subsequent study, however, they demonstrated that alcoholics show greater clearance and lower plasma levels of imipramine than nonalcoholics, suggesting that previous studies which found persistent restlessness and malaise may have utilized dosages that were inadequate for alcoholics (Ciraulo et al. 1982). Future studies should seek to define subtypes of depression in alcoholics, monitor plasma levels of antidepressants, and evaluate drug effects both on depression and on drinking behavior.

Factors Affecting Treatment Outcome

Quality of Treatment

As in other areas of psychotherapy, treatment outcome in alcoholism is affected by the perspectives and attitudes of the therapists, which in turn are functions of their training, experience, and self-esteem (Cartwright 1980). Treatment outcome is also affected by the interpersonal skills of the alcoholism counselor. Valle (1981) evaluated treatment outcomes in patients randomly assigned to eight recovered alcoholic counselors and found that counselors having a higher level of interpersonal functioning tended to have patients who drank less, relapsed less often, and recovered more quickly after a relapse.

Evaluations of training programs for alcoholism counselors indicate that they are able to achieve gains in such areas as participants' knowledge, attitudes, ego strength, capacity for self-disclosure, and effectiveness of counseling (Gideon et al. 1980). The success of alcoholism counselor training programs has prompted their use as a treatment method with chronic alcohol- and drug-dependent individuals, with positive results sustained for at least 1 year (Kahn and Stephen 1981).

Response to Treatment

Treatment research has increasingly focused on identifying personal and environmental factors that predict positive or negative treatment outcomes. Positive outcomes are no longer conceived solely in terms of total abstinence from alcohol, since posttreatment functioning in such domains as physical health, psychological adjustment, social functioning, and occupational performance may not deteriorate automatically with relapse to drinking (Finney et al. 1980); moreover, successful abstinence is not necessarily associated with good functioning in other areas of adjustment.

One form of negative outcome is attrition, that is, failure to complete the treatment program. Client factors found to be related to attrition include inadequate financial resources, low social stability, and youth (Welte et al. 1981; Keil and Esters 1982). Treatment variables such as program duration and size of treatment groups also can influence the

dropout rate (Schroeder et al. 1982). Undoubtedly, attrition results from an interaction between individual and program factors and may be reduced by improvements in program design and the method of assigning patients to treatments.

It is generally believed that treatment outcome is affected less by the treatment process itself than by the personal resources and characteristics the client brings to the treatment situation. Numerous studies have shown good prognosis to be associated with social stability and marital adjustment (Baekeland 1977). Personal characteristics recently reported to be associated with poor prognosis include cognitive impairment (Abbott and Gregson 1981) and depression (Hatsukami et al. 1981). While client characteristics seem to be important determinants of outcome regardless of the quantity or quality of treatment, other research has shown that this effect may be mediated indirectly by the environment to which the client returns after residential treatment (Cronkite and Moos 1980). Another study found that three situational factors (negative mood states, interpersonal conflicts, and social pressure to drink) were most likely to precipitate relapse after treatment (Cummings et al. 1980). These studies indicate that therapeutic efforts must deal not only with the individual characteristics of the patient, but also with the environmental contexts in which the patient is expected to function after treatment.

With this in mind, some have advocated giving more attention to restructuring of the client's environment through marital or family therapy, while others have called for a more general approach focusing on frequent aftercare contact in the period after treatment (Costello 1980). As a neglected dimension in the treatment system, aftercare consists of (a) ongoing supportive activities, such as professional and self-help programs designed to maintain treatment gains, (b) prevention of costly rehospitalizations, and (c) improvement in social and occupational functioning. At present, the resources most frequently available to fulfill these functions are halfway houses, AA groups, and program-sponsored support groups. In general, affiliation with aftercare groups is associated with better treatment outcome (Costello 1980). Further research is needed to determine the relative efficacy of different kinds of aftercare, the optimal frequency and duration of aftercare, and how clients can be induced to comply with aftercare without dropping out.

Matching Patients to Therapies

The emerging concept that alcoholism is not a unitary disorder has stimulated renewed interest in delineating different subgroups or types of alcoholic persons. As discussed previously, the goal of this research is to facilitate treatment planning and improve treatment outcome by matching types of alcoholic persons with the most appropriate treatment interventions. Although this typological approach is not new to the field of alcoholism, recent studies have benefited from improvements in assessment technology (Meyer et al. 1981) and from the application of more sophisticated statistical techniques (Skinner 1982).

Attempts to differentiate alcoholics on the basis of personality characteristics account for most typological research efforts (Morey and Blashfield 1981). Several independent studies have denoted two common subgroups: (1) passive-dependent alcoholic persons characterized by antisocial personality disorder and (2) neurotic alcoholic persons who may use alcohol as a coping mechanism. In a study designed to explore the often-noted association between alcoholism and antisocial (psychopathic) personality, Hesselbrock et al. (in press) compared alcoholics having an early history of social deviance with those who were relatively free from problems before the onset of alcoholism. Alcoholics with antisocial personality were found to have an earlier onset of alcoholism, as well as a more rapid and severe progression of drinking problems. Several other studies (McLellan et al. 1981; Zivich 1981) suggest the importance of psychiatric disturbance, particularly in the alcoholic's response to treatment. Alcoholic subgroups characterized by poor psychological adjustment were found to show little or no improvement following treatment, whereas those having high adjustment levels showed significant improvement. McLellan et al. (1981) conclude that because patients having less severe psychological disturbance respond to most kinds of treatment, cost considerations would recommend this subgroup to outpatient settings.

The probability of a genetic predisposition to alcoholism has prompted the search for an alcoholic subtype related to family pedigree. One study of more than 7,000 alcoholic men found that those with a family history of alcoholism had more severe symptomatology, more antisocial behavior and other psychopathology, less stable employment histories,

and more severe physical symptoms (Frances et al. 1980). Another approach to the classification of alcoholics is based on certain indicators known to predict treatment outcome. One study (Gibbs 1981) classified alcoholics on the dimensions of social stability and intellectual functioning and showed that mutually exclusive types were often assigned to the same treatment regimen despite their widely different rehabilitation needs.

In an attempt to directly test the clinical implications of differentiating subgroups of alcoholics, several investigators have studied how certain types of patients respond to different treatments. Using a classification system that differentiates chronic alcoholics from a less severe type of behaviorally impaired drinker, Brown and Lyons (1981) found that alcoholics do slightly better in programs having a high medical orientation, while the behaviorally impaired drinkers respond better to treatment having a high psychological rehabilitation orientation. Using a different classification scheme, Finney and Moos (1979) studied the treatment response of alcoholics classified in terms of high or low social competence. Contrary to the findings of Brown and Lyons (1981), no evidence was found to indicate that various treatment programs were differentially effective for different types of patients.

Although evidence supporting treatment matching remains equivocal, there may be important methodological reasons why the matching hypothesis has not been adequately tested. First, despite improvements in the methods and theory of classification, the optimal classification system has yet to be developed. Even though family history, psychiatric disorder, alcoholic symptomatology, and organic brain dysfunction seem to be promising differentiating characteristics, there has been little attempt to integrate information from these disparate levels of analysis into more comprehensive typologies. Second, many matching studies have not been designed to detect predicted interactions. In a recent review of the matching literature (Skinner 1981), it was found that evidence supporting the matching hypothesis came primarily from those experimental studies that randomly assigned patients to treatment conditions, while the results of nonexperimental correlational studies tended to be less supportive. Finally, in a number of studies it is possible that the assigned treatments were not sufficiently distinct to produce a differential effect. Thus, while the matching hypothesis still holds promise as an avenue to improved treatment efficacy, the systematic study of patient-treatment interactions will have to await the development of better typologies and improved scientific research methodology.

Emerging Trends and Future Directions

A consensus appears to be developing among clinicians, researchers, and policymakers that treatment research is passing through a transitional period during which basic assumptions are being reevaluated and a new approach to treatment efficacy is emerging. The elements of this trend include refinements in the definition of terms, improvements in the technology of diagnosis, a more sophisticated approach to the planning of treatments, and a new awareness of the complexity of evaluation methodology.

The advances noted in this chapter in the areas of conceptualization, assessment, and treatment intervention can only serve to enhance the quality of services available to alcoholic persons. The notion that different degrees of alcohol dependence can be measured, that different types of alcoholic persons can be classified, and that different types of disability can be diagnosed has important implications for treatment and research. Recent reviews of treatment-related priorities conducted by the Institute of Medicine (1980), the Journal of Studies on Alcohol (Keller 1979), and the World Health Organization (Edwards et al. 1981) suggest that these themes will constitute a promising but ambitious agenda for the 1980s. As articulated in the writings of many specialists in the field, a new approach is emerging regarding the ways in which treatment is conceptualized, conducted, and evaluated.

The traditional model, which still dominates much thinking about alcoholism treatment, describes how heterogeneous groups of patients are assigned to multimodal treatment programs. After a period of time, the relative success or failure of treatment is evaluated primarily on the basis of the proportion of patients remaining abstinent, and secondarily by global assessments of functioning in other areas of living. Because both treatment variables and client variables are aggregated in this approach, treatment effects may be obscured when the improvements of some patients are averaged with the lack of improvement or even deterioration of other patients. Even when treatment effects are observed, it

is not clear which parts of the treatment process are responsible. In addition to the conceptual limitations of this model, much of the evaluation research conducted within this tradition is difficult to interpret because patient characteristics differ from one study to another, outcome criteria have not been sufficiently specified, comparison groups have not been included in the research design, and the treatment process has not been adequately described. Furthermore, the posttreatment environment has not been taken into account, and there have been unrealistic expectations about what the treatment will accomplish.

In contrast to the traditional model of treatment, the emerging model stresses the heterogeneous nature of the client population, the need for more specific and efficient interventions, the importance of maintaining treatment gains in the posttreatment environment, and the diversities of different outcomes (Skinner 1981; Cronkite and Moos 1980). This model differentiates among types of alcoholic persons (e.g., less dependent or more dependent, depressed or not depressed, cognitively impaired or not impaired) and conjointly attempts to match each type with the most appropriate combination of treatment interventions (e.g., pharmacotherapy, behavior therapy, family treatment, etc.). The efficacy of various treatment combinations is evaluated by comparing patients who are matched to appropriate treatments with those who are mismatched or assigned randomly to a standard package of interventions. Within the new model, greater attention is given to evaluating changes in behavior, attitudes, physical health, and psychosocial functioning taking place during the process of treatment. Another area of focus is the posttreatment environment, where the patient's recovery may be impeded or supported by what takes place in the family setting or in the job situation. Ideally, the treatment process would continue during the posttreatment period in the form of various kinds of specialized aftercare. Finally, the new model recognizes that outcome may vary along a variety of dimensions, and that abstinence is just one goal of a more ambitious treatment strategy that includes rehabilitation in other important areas of functioning.

Summary

The traditional concept of alcoholism as a unitary disease has been challenged. Over the past decade, researchers and clinicians have come to realize that multiple patterns of alcohol use may result in multiple forms of disability. Accordingly, a new emerging model of treatment stresses the heterogeneous nature of the client population, the need for more specific and efficient treatments, and the importance of maintaining gains after treatment. This model differentiates among alcoholics (e.g., depressed vs. nondepressed) and attempts to match each type with the most appropriate combination and configuration of treatments.

Recognizing the importance of accurate patient descriptions, the American Psychiatric Association has developed systematic criteria for classifying alcoholic patients along a number of dimensions. The technique, a part of DSM III (Diagnostic and Statistical Manual of Mental Disorders) promises to provide more standardized and comprehensive patient diagnoses.

Several methods are currently used to identify alcoholics before they come for treatment. Laboratory tests for biological markers or indicators can be a powerful aid to detecting alcoholism. Current research on the use of biochemical indicators in the early detection of alcoholism suggests that a single specific biochemical marker for alcoholism may be elusive. The combination of GGTP, MCV, and several other tests, however, appears to offer, at relatively low cost, a strong indication of recent excessive alcohol consumption. In addition, a widely used and validated self-administered test, the Michigan Alcoholism Screening Test (MAST), elicits responses to medical, social, and behavioral statements. The MAST is rapid, inexpensive, and relatively accurate.

Studies show that untreated alcoholics and their families are disproportionately high users of medical services. Insurance programs, especially HMOs, in recognition of the cost implications have begun to target alcoholism for increased attention. Preliminary studies suggest that partial hospitalization or outpatient programs may be as effective as inpatient programs for some patients; moreover, the lower costs of the former may lead to increased use.

Treatments continue to rely largely on psychotherapy and behavior therapy (including social skills and assertiveness training, self-control training, cognitive restructuring, and aversion therapy, which pairs alcohol with unpleasant stimuli). In addition, group approaches like Alcoholics Anonymous are widespread. Behavior therapy in conjunction

with disulfiram (Antabuse) seems to be highly effective in producing abstinence; however, abstinence alone does not imply successful psychosocial adjustment.

References

Abbott, M.W., and Gregson, R.A.M. Cognitive dysfunction in the prediction of relapse in alcoholics. Journal of Studies on Alcohol 42(3): 230-243, 1981.

Alcoholics Anonymous, General Service Office. Analysis of the 1980 Survey of the Membership of A.A. New York: AA, 1981. 18 pp.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. (DSM III). 3rd ed. Washington, D.C.: APA, 1980.

Armor, D.J.; Polich, J.M.; and Stambul, H.B. Alcoholism and Treatment. New York: John Wiley & Sons, 1978.

Azrin, N.H.; Sisson, R.W.; Meyers, S.B.; and Godley, M. Alcoholism treatment by disulfiram and community reinforcement therapy. Journal of Behaviour Therapy and Experimental Psychiatry 13(2):105-112, 1982.

Babor, T.F.; Treffardier, M.; Weill, J.; Fegueur, L.; and Ferrant, J-P. Early detection and the secondary prevention of alcoholism in France: A quoi bon? Journal of Studies on Alcohol 44(4): 600-616, 1983.

Baekeland, F. Evaluation of treatment methods in chronic alcoholism. In: Kissin, B., and Begleiter, H., eds. Treatment and Rehabilitation of the Chronic Alcoholic. New York: Plenum Press, 1977. pp. 385-440.

Bean, M.H., and Zinberg, N.E., eds. Dynamic Approaches to the Understanding and Treatment of Alcoholism. New York: Free Press, 1981. 214 pp.

Beckman, L.J., and Kocel, K.M. The treatment-delivery system and alcohol abuse in women: Social policy implications. Journal of Social Issues 38(2):139-151, 1982.

Beyer, J.M.; Trice, H.M.; and Hunt, R.E. The impact of Federal sector unions on supervisors' use of personnel policies. Industrial Labor Relations Review 33:212-231, 1980.

Blakey, R., and Baker, R. An exposure approach to alcohol abuse. Behaviour Research and Therapy 18:319-325, 1980.

Boscarino, J. Factors related to "stable" and "unstable" affiliation with Alcoholics Anonymous. International Journal of the Addictions 15(6): 839-848, 1980.

Brady, J.P.; Foulks, E.T.; Childress, A.R.; and Pertschuk, M. The Michigan Alcoholism Screening Test as a survey instrument. Journal of Operational Psychiatry 13(1):27-31, 1982.

Brown, J., and Lyons, J.P. A progressive diagnostic schema for alcoholism with evidence of clinical efficacy. Alcoholism: Clinical and Experimental Research 5(1):17-25, 1981.

Cannon, D.S.; Baker, T.B.; and Wehl, C.K. Emetic and electric shock alcohol aversion therapy: Six- and twelve-month follow-up. Journal of Consulting and Clinical Psychology 49(3):360-368, 1981.

Cartwright, A.K.J. The attitudes of helping agents towards the alcoholic client: The influence of experience, support, training, and self-esteem. British Journal of Addiction 75(4):413-431, 1980.

Chaney, E.; O'Leary, M.; and Marlatt, G.A. Skill training with alcoholics. Journal of Consulting and Clinical Psychology 46(5):1092-1104, 1978.

Chick, J.; Kreitman, N.; and Plant, M. Mean cell volume and gamma-glutamyl-transpeptidase as markers of drinking in working men. Lancet 1:1249-1251, 1981.

Chick, J.; Lloyd, G.; and Crombie, E. "Natural History and Effect of Minimal Intervention in Newly Identified Problem Drinkers in a General Hospital." Paper presented at 33rd International Congress on Alcoholism and Drug Dependence, Tangier, Morocco, October 1982.

Ciraulo, D.A., and Jaffe, J.H. Tricyclic antidepressants in the treatment of depression associated with alcoholism. Journal of Clinical Psychopharmacology 1(3):146-150, 1981.

Ciraulo, D.A.; Lloyd, M.A.; Chapron, D.J.; Jaffe, J.H.; Subbarao, B.; and Kramer, P.A. Imipramine disposition in alcoholics. Journal of Clinical Psychopharmacology 2(1):2-7, 1982.

Cole, S.G.; Lehman, W.E.; Cole, E.A.; and Jones, A. Inpatient vs. outpatient treatment of alcohol and drug abusers. American Journal of Drug and Alcohol Abuse 8(3):329-345, 1981.

Costello, R.M. Alcoholism aftercare and outcome: Cross-lagged panel and path analyses. British Journal of Addiction 75:49-53, 1980.

Costello, R.M., and Baillargeon, J.G. Reliability analysis of the treatment difficulty scale. American Journal of Drug and Alcohol Abuse 8(1):117-121, 1981.

Cronkite, R.C., and Moos, R.H. Determinants of the posttreatment functioning of alcoholic patients: A conceptual framework. Journal of Consulting and Clinical Psychology 48(3):305-316, 1980.

Cummings, C.; Gordon, J.R.; and Marlatt, G.A. Relapse: Prevention and prediction. In: Miller, W.R., ed. The Addictive Behaviors: Treatment of Alcoholism, Drug Abuse, Smoking and Obesity. New York: Pergamon Press, 1980. pp. 291-321.

Den Hartog, G.L. "A Decade of Detox": Development of Non-Hospital Approaches to Alcohol Detoxification - A Review of the Literature. Substance Abuse Monograph Series. Jefferson City, Mo.: Division of Alcohol and Drug Abuse, 1982. 67 pp.

Diesenhaus, H. Current trends in treatment programing for problem drinkers and alcoholics. In: National Institute on Alcohol Abuse and Alcoholism. Prevention, Intervention and Treatment: Concerns and Models. Alcohol and Health Monograph No. 3. DHHS Pub. No. (ADM) 82-1192. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 219-290.

Edwards, G.; Arif, A.; and Hodgson, R. Nomenclature and classification of drug- and alcohol-

related problems: A WHO memorandum. Bulletin of the World Health Organization 59(2):223-242, 1981.

Edwards, G.; Gross, M.M.; Keller, M.; and Moser, J., eds. Alcohol-related problems in the disability perspective. Journal of Studies on Alcohol 37(9):1360-1382, 1976.

Edwards, G.; Orford, J.; Egert, S.; Guthrie, S.; Hawker, A.; Hensman, C.; Mitcheson, M.; Oppenheimer, E.; and Taylor, C. Alcoholism: A controlled trial of "treatment" and "advice." Journal of Studies on Alcohol 38(5):1004-1031, 1977.

Elkins, R.L. Covert sensitization treatment of alcoholism: Contributions of successful conditioning to subsequent abstinence maintenance. Addictive Behaviors 5(1):67-89, 1980.

Fagan, R.W., and Mauss, A.L. Padding the revolving door: An initial assessment of the Uniform Alcoholism and Intoxication Treatment Act in practice. Social Problems 26(2):232-247, 1978.

Feighner, J.P.; Robins, E.; Guze, S.B.; Woodruff, R.A.; Winokur, G.; and Munoz, R. Diagnostic criteria for use in psychiatric research. Archives of General Psychiatry 26:57-63, 1972.

Ferrell, W.L., and Galassi, J.P. Assertion training and human relations training in the treatment of chronic alcoholics. International Journal of the Addictions 16(5):959-968, 1981.

Finney, J.W., and Moos, R.H. Treatment and outcome for empirical subtypes of alcoholic patients. Journal of Consulting and Clinical Psychology 47(1):25-38, 1979.

Finney, J.W., and Moos, R.H. Characteristics and prognoses of alcoholics who become moderate drinkers and abstainers after treatment. Journal of Studies on Alcohol 42(1):94-105, 1981.

Finney, J.W.; Moos, R.H.; and Mewborn, C.R. Posttreatment experiences and treatment outcome of alcoholic patients six months and two years after hospitalization. Journal of Consulting and Clinical Psychology 48(1):17-29, 1980.

Forsythe, A.B.; Griffiths, B.; and Reiff, S. Comparison of utilization of medical services by alcoholics and non-alcoholics. American Journal of Public Health 72(6):600-602, 1982.

Frances, R.J.; Timm, S.; and Bucky, S. Studies of familial and nonfamilial alcoholism. Archives of General Psychiatry 37:564-566, 1980.

Freedberg, E.J., and Johnston, W.E. Outcome with alcoholics seeking treatment voluntarily or after confrontation by their employer. Journal of Occupational Medicine 22:83-86, 1980.

Fuller, R.K., and Roth, H.P. Disulfiram for the treatment of alcoholism: An evaluation in 128 men. Annals of Internal Medicine 90(6):901-904, 1979.

Fuller, R.K., and Williford, W.O. Life-table analysis of abstinence in a study evaluating the efficacy of disulfiram. Alcoholism: Clinical and Experimental Research 4(3):298-301, 1980.

Garvin, R.B.; Foy, D.W.; and Alford, G.S. A critical examination of gamma-glutamyl transpeptidase as a biochemical marker for alcohol abuse. Addictive Behaviors 6:377-383, 1981.

Gibbs, L.E. The need for a new design for evaluating alcoholism treatment programs. Drug and Alcohol Dependence 8(4):287-299, 1981.

Gideon, W.L.; Littell, A.S.; and Martin, D.W. Evaluation of a training program for certified alcoholism counselors. Journal of Studies on Alcohol 41(1):8-20, 1980.

Glaser, F.B., and Ogborne, A.C. What we most like to know: Does A.A. really work? British Journal of Addiction 77(2):123-129, 1982.

Googins, B., and Kurtz, N.R. Factors inhibiting supervisory referrals to occupational alcoholism intervention programs. Journal of Studies on Alcohol 41(11):1196-1208, 1980.

Hatsukami, D.; Pickens, R.W.; and Svikis, D. Posttreatment depressive symptoms and relapse to drug use in different age groups of an alcohol and other drug abuse population. Drug and Alcohol Dependence 8(4):271-277, 1981.

Heather, N., and Robertson, I. Controlled Drinking. London: Methuen, 1981. 294 pp.

Helzer, J.E. "Methodologies and Data to Measure Numbers of Alcoholics." Paper presented at the 34th ADPA annual conference, Washington, D.C., August 30, 1983.

Helzer, J.E.; Robins, L.N.; Croughan, J.L.; and Welner, A. Renard Diagnostic Interview: Its reliability and procedural validity with physicians and lay interviewers. Archives of General Psychiatry 38(4):393-398, 1981.

Hesselbrock, M.; Babor, T.F.; Hesselbrock, V.; Meyer, R.E.; and Workman, K. "Never believe an alcoholic?" On the validity of self-report measures of alcohol dependence and related constructs. International Journal of the Addictions 18(5):593-609, 1983.

Hesselbrock, M.N.; Hesselbrock, V.M.; Babor, T.F.; Stabenau, J.R.; Meyer, R.E.; and Weidenman, M. Antisocial behavior, psychopathology and problem drinking in the natural history of alcoholism. In: Goodwin, D.W.; Van Dusen, K.; and Mednick, S.A., eds. Longitudinal Studies of Alcoholism. Copenhagen, Denmark: Nijhoff Publishing Co., in press.

Hesselbrock, V.; Stabenau, J.; Hesselbrock, M.; Mirkin. P.; and Meyer, R. A comparison of two interview schedules: The schedule for affective disorders and schizophrenia-lifetime and the National Institute of Mental Health Diagnostic Interview Schedule. Archives of General Psychiatry 39(6):674-677, 1982.

Hinson, R.E., and Siegel, S. The contribution of Pavlovian conditioning to ethanol tolerance and dependence. In: Rigter, H., and Crabbe, J.C., eds. Alcohol Tolerance and Dependence. Amsterdam: Elsevier/North-Holland Biomedical, 1980. pp. 181-199.

Holder, H.D., and Hallan, J.B. Medical Care and Alcoholism Treatment Costs and Utilization: A Five-Year Analysis of the California Pilot Project to Provide Health Insurance Coverage for Alcoholism. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1981. 57 pp.

Institute of Medicine. Alcoholism, Alcohol Abuse, and Related Problems: Opportunities for Re-

search. Publication IOM 80-04. Washington, D.C.: National Academy Press, 1980. 195 pp.

Jones, K.R., and Vischi, T.R. Impact of alcohol, drug abuse and mental health treatment on medical care utilization: A review of the research literature. Medical Care 17 (12, Supplement): 1-82, 1979.

Jones, S.L.; Kanfer, R.; and Lanyon, R.I. Skill training with alcoholics: A clinical extension. Addictive Behaviors 7(3):285-290, 1982.

Kahn, M.W., and Stephen, L.S. Counselor training as a treatment method for alcohol and drug abuse. International Journal of the Addictions 16(8):1415-1424, 1981.

Kaplan, R.F.; Meyer, R.E.; and Stroebel, C.F. The symptoms of alcohol withdrawal as predictors of behavioral and physiological responses to an ethanol stimulus. In: National Institute on Drug Abuse. Problems of Drug Dependence 1982. Louis S. Harris, ed. Research Monograph Series 43. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1983. pp. 273-279.

Keil, T.J., and Esters, R.A. Treatment dropouts: The effect of client and ecological variables. International Journal of the Addictions 17(1): 93-108, 1982.

Keller, M., ed. Research priorities on alcohol. Proceedings of a symposium sponsored by the Rutgers Center of Alcohol Studies and Rutgers University. Journal of Studies on Alcohol. Supplement No. 8, November 1979. 342 pp.

Kissin, B. Patient characteristics and treatment specificity in alcoholism. In Idestrom, C-M., ed. Recent Advances in the Study of Alcoholism. Amsterdam: Excerpta Medica, 1977. pp. 110-122.

Kline, N.S.; Wren, J.C.; Cooper, T.B.; Varga, E.; and Canal, O. Evaluation of lithium therapy in chronic and periodic alcoholism. American Journal of the Medical Sciences 268(1):15-22, 1974.

Kristenson, H. "Studies on Alcohol Related Disabilities in a Medical Intervention Programme in Middle-aged Males." Doctoral dissertation, Lund University, Sweden, 1982.

Kurtz, N.R.; Googins, B.; and Williams, C. Clients' views of an alcoholism program. Labor-Management Alcoholism Journal 10(3):102-113, 1980.

Longabaugh, R.; McCrady, B.; Fink, E.: and Stout, R. Cost effectiveness of alcoholism treatment in partial vs. inpatient settings: Six month outcomes. Journal of Studies on Alcohol, in press.

Marlatt, G.A. The drinking history: Problems of validity and reliability. In: Meyer, R.E.; Babor, T.F.; Glueck, B.C.; Jaffe, J.H.; O'Brien, J.E.; and Stabenau, J.R., eds. Evaluation of the Alcoholic: Implications for Research, Theory and Treatment. NIAAA Research Monograph No. 5. DHHS Pub. No. (ADM)81-1033. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981. pp. 25-39.

Mayfield, D.G., and Johnston, R.G.M. Screening techniques and prevalence estimation in alcoholism. In: Fann, W.E.; Karacan, I.; Pokorny, A.D.; and Williams, R.L., eds. Phenomenology and Treatment of Alcoholism. New York: Spectrum Publishers, 1980. pp. 33-44.

McCrady, B.S., and Noel, N.E. "Assessing the Optimal Mode of Spouse Involvement in Outpatient Behavioral Alcoholism Treatment." Paper presented at the 16th Annual Meeting of the Association for the Advancement of Behavior Therapy, Los Angeles, November 1982.

McIntosh, I.D. Alcohol-related disabilities in general hospital patients: A critical assessment of the evidence. International Journal of the Addictions 17(4):609-639, 1982.

McLachlan, J.F.C., and Stein, R.L. Evaluation of a day clinic for alcoholics. Journal of Studies on Alcohol 43(3):261-278, 1982.

McLellan, A.T.; Luborsky, L.; Woody, G.E.; and O'Brien, C.P. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. Journal of Nervous and Mental Disease 168(1):26-33, 1980.

McLellan, A.T.; Luborsky, L.; Woody, G.E.; O'Brien, C.P.; and Kron, R. Are the "addiction-related" problems of substance abusers really related? Journal of Nervous and Mental Disease 169(4):232-239, 1981.

McMillan, T.M. Lithium and the treatment of alcoholism: A critical review. British Journal of Addiction 76(3):245-258, 1981.

Meyer, R.E.; Babor, T.F.; Glueck, B.C.; Jaffe, J.H.; O'Brien, J.E.; and Stabenau, J.R., eds. Evaluation of the Alcoholic: Implications for Research, Theory and Treatment. NIAAA Research Monograph No. 5. DHHS Pub. No. (ADM)81-1033. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981. 409 pp.

Miller, P. M., and Mastria, M.A. Alternatives to Alcohol Abuse: A Social Learning Model. Champaign, Ill.: Research Press, 1977. 190 pp.

Miller, W.R., and Hester, R.K. Treating the problem drinker: Modern approaches. In: Miller, W.R., ed. The Addictive Behaviors: Treatment of Alcoholism, Drug Abuse, Smoking, and Obesity. New York: Pergamon Press, 1980. pp. 11-141.

Miller, W.R.; Taylor, C.A; and West, J.C. Focused versus broad-spectrum behavior therapy for problem drinkers. Journal of Consulting and Clinical Psychology 48(5):590-601, 1980.

Moberg, D.P.; Krause, W.K.; and Klein, P.E. Post-treatment drinking behavior among inpatients from an industrial alcoholism program. International Journal of the Addictions 17(3):549-567, 1982.

Moos, R.H.; Finney, J.W.; and Chan, D.A. The process of recovery from alcoholism. I. Comparing alcoholic patients and matched community controls. Journal of Studies on Alcohol 42(5):383-402, 1981.

Morey, L.C., and Blashfield, R.K. Empirical classifications of alcoholism: A review. Journal of Studies on Alcohol 42(11):925-937, 1981.

Mulford, H.A. On the validity of the Iowa Alcoholic Stages Index. Journal of Studies on Alcohol 41(1):86-88, 1980.

Mulford, H.A., and Fitzgerald, J.L. On the validity of the Research Diagnostic Criteria, the Feighner Criteria, and the DSM-III for diagnosing al-

coholics. Journal of Nervous and Mental Disease 169(10):654-658, 1981.

National Institute on Alcohol Abuse and Alcoholism. National Drug and Alcoholism Treatment Utilization Survey. Executive Report. Rockville, Md.: NIAAA, September 1980. 9 pp. and appendixes.

National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM) 82-1193. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. 446 pp.

Neiderhiser, D.H., and Fuller, R.K. High-performance liquid chromatographic method for the determination of diethylamine, a metabolite of disulfiram, in urine. Journal of Chromatography 229(2):470-474, 1982.

Oei, T.P.S., and Jackson, P. Long-term effects of group and individual social skills training with alcoholics. Addictive Behaviors 5:129-136, 1980.

Oei, T.P.S., and Jackson, P. Social skills and cognitive behavioral approaches to the treatment of problem drinking. Journal of Studies on Alcohol 43(5):532-547, 1982.

O'Farrell, T.J.; Harrison, R.H.; Schulmeister, C.A.; and Cutter, H.S. Closeness to Divorce Scale for wives of alcoholics. Drug and Alcohol Dependence 7(4):319-324, 1981.

Ogborne, A.C., and Glaser, F.B. Characteristics of affiliates of Alcoholics Anonymous: A review of the literature. Journal of Studies on Alcohol 42(7):661-675, 1981.

O'Leary, M.R.; Calsyn, D.A.; Haddock, D.L.; and Freeman, C.W. Differential alcohol use patterns and personality traits among three Alcoholics Anonymous attendance level groups: Further considerations of the affiliation profile. Drug and Alcohol Dependence 5:135-144, 1980.

Olson, R.P.; Devine, V.T.; Ganley, R.; and Dorsey, G.C. Long-term effects of behavioral versus insight-oriented therapy with inpatient alcoholics. Journal of Consulting and Clinical Psychology 49(6):866-877, 1981.

Orford, J.; Oppenheimer, E.; and Edwards, G. Abstinence or control: The outcome for excessive drinkers two years after consultation. Behaviour Research and Therapy 14(6):409-418, 1976.

Pattison, E.M. Nonabstinent drinking goals in the treatment of alcoholism: A clinical typology. Archives of General Psychiatry 33(8):923-930, 1976.

Pattison, E.M., and Kaufman, E. Family therapy in the treatment of alcoholism. In: Lansky, M.W., ed. Family Therapy and Major Psychopathology. New York: Grune & Stratton, 1981. pp. 203-229.

Paulson, S.M.; Krause, S.; and Iber, F.L. Development and evaluation of a compliance test for patients taking disulfiram. Johns Hopkins Medical Journal 141(3):119-125, 1977.

Plotnick, D.E.; Adams, K.M.; Hunter, H.R.; and Rowe, J.C. Alcoholism Treatment Programs Within Prepaid Group Practice HMOs: A Final Report. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1982. 130 pp. and appendixes.

Polich, J.M.; Armor, D.J.; and Braiker, H.B. The Course of Alcoholism: Four Years After Treatment. New York: John Wiley & Sons, 1981. 334 pp.

Pomerleau, O.F.; Fertig, J.; Baker, L.; and Cooney, N. Reactivity to alcohol cues in alcoholics and non-alcoholics: Implications for a stimulus control analysis of drinking. Addictive Behaviors 8(1):1-10, 1983.

Pomerleau, O.F.; Pertschuk, M.; Adkins, D.; and Brady, J.P. A comparison of behavioral and traditional treatment methods for middle-income problem drinkers. Journal of Behavioral Medicine 1:187-200, 1978.

Pond, S.M.; Becker, C.E.; Vandervoort, R.; Phillips, M.; Bowler, R.M.; and Peck, C.C. An evaluation of the effects of lithium in the treatment of chronic alcoholism. I. Clinical results. Alcoholism: Clinical and Experimental Research 5(2): 247-251, 1981.

Putnam, S.L. Alcoholism, morbidity and care-seeking: The inpatient and ambulatory service utilization and associated illness experience of alcoholics and matched controls in a health maintenance organization. Medical Care 20(1): 97-121, 1982a.

Putnam, S.L. Short-term effects of treating alcoholics for alcoholism: Utilization of medical care services by alcoholics in a health maintenance organization. The Group Health Journal 3(1): 19-30, 1982b.

Reyes, E., and Miller, W.R. Serum gamma-glutamyl transpeptidase as a diagnostic aid in problem drinkers. Addictive Behaviors 5:59-65, 1980.

Richman, A., and Smart, R.G. After how many detoxifications is rehabilitation probable? Drug and Alcohol Dependence 7(3):233-238, 1981.

Robichaud, C.; Strickler, D.; Bigelow, G.; and Liebson, I. Disulfiram maintenance employee alcoholism treatment: A three-phase evaluation. Behavior Research and Therapy 17(6):618-621, 1979.

Roghmann, K.J.; Roberts, J.S.; Smith, T.S.; Wells, S.M.; and Wersinger, R.P. Alcoholics' versus nonalcoholics' use of services of a health maintenance organization. Journal of Studies on Alcohol 42(3):312-322, 1981.

Roman, P.M. Barriers to the use of constructive confrontation with employed alcoholics. Journal of Drug Issues 12(4):369-382, 1982.

Roman, P. From employee alcoholism to employee assistance: De-emphases on prevention and alcohol problems in work-based programs. Journal of Studies on Alcohol 42(3):244-272, 1981.

Ryback, R.S.; Eckardt, M.J.; Felsher, B.; and Rawlings, R.R. Biochemical and hematologic correlates of alcoholism and liver disease. Journal of the American Medical Association 248(18):2261-2265, 1982.

Ryback, R.S.; Eckardt, M.J.; and Pautler, C.P. Biochemical and hematological correlates of alcoholism. Research Communications in Chemical Pathology and Pharmacology 27(3):533-550, 1980.

Sanchez-Craig, M., and Walker, K. Teaching coping skills to chronic alcoholics in a coeducational halfway house: I. Assessment of programme effects. British Journal of Addiction 77(1):35-50, 1982.

Saxe, L.; Dougherty, D.; Esty, K.; and Fine, M. The Effectiveness and Costs of Alcoholism Treatment. Health Technology Case Study 22. Report No. OTA-HCS-22. Washington, D.C.: Congress of the United States, Office of Technology Assessment, 1983. 108 pp.

Schroeder, D.J.; Bowen, W.T.; and Twemlow, S.W. Factors related to patient attrition from alcoholism treatment programs. International Journal of the Addictions 17(3):463-472, 1982.

Skinner, H.A. Different strokes for different folks: Differential treatment for alcohol abuse. In: Meyer, R.E.; Babor, T.F.; Glueck, B.C.; Jaffe, J.H.; O'Brien, J.E.; and Stabenau, J.R., eds. Evaluation of the Alcoholic: Implications for Research, Theory and Treatment. NIAAA Research Monograph No. 5. DHHS Pub. No. (ADM) 81-1033. Washington, D.C.; Supt. of Docs., U.S. Govt. Print. Off., 1981. pp.349-367.

Skinner, H.A. Statistical approaches to the classification of alcohol and drug addiction. British Journal of Addiction 77(3):259-273, 1982.

Skinner, H.A., and Allen, B.A. Alcohol dependence syndrome: Measurement and validation. Journal of Abnormal Psychology 91(3):199-209, 1982.

Skinner, H.A.; Holt, S.; Allen, B.A.; and Haakonson, N.H. Correlation between medical and behavioral data in the assessment of alcoholism. Alcoholism: Clinical and Experimental Research 4(4):371-377, 1980.

Skinner, H.A.; Holt, S.; and Israel, Y. Early identification of alcohol abuse: I. Critical issues and psychosocial indicators for a composite index. Canadian Medical Association Journal 124(9): 1141-1152, 1981.

Sokolow, L.; Welte, J.; Hynes, G.; and Lyons, J. Multiple substance use by alcoholics. British Journal of Addiction 76(2):147-158, 1981.

Spicer, J.; Nyberg, L.R.; and McKenna, T.R. Apples and Oranges: A Comparison of Inpatient and Outpatient Programs. Center City, Minn.: Hazelden Foundation, 1981.

Spitzer, R.L.; Williams, J.B.W.; and Skodol, A.E. DSM-III: The major achievements and an overview. American Journal of Psychiatry 137(2): 151-164, 1980.

Stanton, M.D., and Todd, T.C. The Family Therapy of Drug Abuse and Addiction. New York: Guilford Press, 1982.

Steinglass, P. Family therapy with alcoholics: A review. In: Kaufman, E., and Kaufmann, P.N., eds. Family Therapy of Drug and Alcohol Abuse. New York: Gardner Press, 1979. pp. 147-186.

Stockwell, T.; Hodgson, R.; Edwards, G.; Taylor, C.; and Rankin, H. The development of a questionnaire to measure severity of alcohol dependence. British Journal of Addiction 74:79-87, 1979.

Strickler, D.P.; Bradlyn, A.S.; and Maxwell, W.A. Teaching moderate drinking behaviors to young adult heavy drinkers: The effects of three training procedures. Addictive Behaviors 6(4): 355-364, 1981.

Swint, J.M., and Nelson, W.B. Prospective evaluation of alcoholism rehabilitation efforts: The role of cost-benefit and cost-effectiveness analyses. Journal of Studies on Alcohol 38(7): 1386-1404, 1977.

U.S. Department of Health and Human Services. Fourth Special Report to the U.S. Congress on Alcohol and Health. DeLuca, J.R., ed. DHHS Pub No. (ADM)81-1080. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

Vaillant, G.E. Dangers of psychotherapy in the treatment of alcoholism. In: Bean, M.H., and Zinberg, N.E., eds. Dynamic Approaches to the Understanding and Treatment of Alcoholism. New York: Free Press, 1981. pp. 36-54.

Valle, S.K. Interpersonal functioning of alcoholism counselors and treatment outcome. Journal of Studies on Alcohol 42(9):783-790, 1981.

Vannicelli, M. Group psychotherapy with alcoholics: Special techniques. Journal of Studies on Alcohol 43(1):17-37, 1982.

Wallace, J. Working with the preferred defense structure of the recovering alcoholic. In: Zimberg, S.; Wallace, J.; and Blume, S.B., eds. Practical Approaches to Alcoholism Psychotherapy. New York: Plenum, 1978. pp. 19-29.

Weissman, M.M.; Meyers, J.K.; and Harding, P.S. Prevalence and psychiatric heterogeneity of alcoholism in a United States urban community. Journal of Studies on Alcohol 41(7):672-681, 1980.

Welte, J.W.; Hynes, G.; Sokolow, L.; and Lyons, J.P. Comparison of clients completing inpatient alcoholism treatment with clients who left prematurely. Alcoholism: Clinical and Experimental Research 5(3):393-399, 1981.

Wilkinson, D.A., and Sanchez-Craig, M. Relevance of brain dysfunction to treatment objectives: Should alcohol-related cognitive deficits influence the way we think about treatment? Addictive Behaviors 6(3):253-260, 1981.

World Health Organization. Diagnosis and Classification of Mental Disorders and Alcohol and Drug-Related Problems. Summaries of working papers from an international conference, Copenhagen, Denmark, April 1982.

Zimberg, S. Office psychotherapy of alcoholism. In: Solomon, J., ed. Alcoholism and Clinical Psychiatry. New York: Plenum Medical Books, 1982. pp. 213-229.

Zivich, J.M. Alcoholic subtypes and treatment effectiveness. Journal of Consulting and Clinical Psychology 49(1):72-80, 1981.

Chapter VIII

Prevention: A Broad Perspective

This chapter will describe current perspectives on prevention of alcohol-related problems, summarize recent research findings, and highlight activities at national, State, and community levels to reduce alcohol-related problems.

Current Perspectives

Within recent years, prevention of alcohol-related problems has emerged as a key issue not only in the United States but internationally as well (Mosher 1981). There has been enormous growth of attention on the part of many countries as it becomes increasingly clear that few, if any, countries are free of problems associated with the consumption of alcohol. Legislators, educators, researchers, and others throughout the world are seeking ways to reduce alcohol-related problems and to decrease the personal, social, and economic costs associated with them.

The emerging focus on prevention is related to a number of factors. One is the realization that the treatment system alone cannot be expected to deal with all alcohol-related problems (USDHHS 1981). Another is that not only heavy chronic drinkers cause and suffer from alcohol problems. The National Academy of Sciences' report, Alcohol and Public Policy: Beyond the Shadow of Prohibition (Moore and Gerstein 1981), indicates that:

> Chronic drinkers with high consumption both cause and suffer far more than their numerical share of the adverse consequences of drinking, (but) their share of alcohol problems is still only a fraction--typically less than half--of the total. Alcohol problems occur throughout the drinking population . . . at lower rates but among much greater numbers as one moves from the heaviest drinkers to more moderate drinkers. (p. 44)

In addition, significant grassroots groups concerned about alcohol problems have developed over the past few years. Some of these have focused national attention on and stimulated nationwide action to reduce alcohol-related highway accidents. Others have focused on education, mutual support groups, server responsibility, concern about alcohol beverage advertising, and support for additional enforcement and legislative actions that have prevention potential.

Empirical research on alcohol-related problems among special population groups (e.g., women, young black men, Hispanic Americans, American Indians and Native Alaskans, and the elderly) indicates a need for and has contributed to a growing interest in prevention efforts for specific at-risk populations.

Furthermore, research in a number of areas offers significant promise for future prevention efforts. These areas include:

- The effects of alcohol consumption on neurotransmitters in the nervous system
- Means for manipulating tolerance to alcohol in the brain
- Genetic factors or markers that may help to explain why individuals seem to differ in their vulnerabilities to the problems associated with alcohol consumption
- Role of known risk factors in the development of alcohol-related problems
- Assessment of the impact of legislative and regulatory measures
- Early identification and diagnosis of alcohol problems
- Increased awareness of the need to further evaluate various educational and community approaches

Since the Fourth Special Report to Congress (USDHHS 1981), there appears to have developed an emerging consensus that the public health approach can provide a useful conceptual framework for developing prevention strategies. This model derives from epidemiological studies of communicable disease indicating that proper planning requires knowledge not only of host, agent, and environment, but also of their interaction.

Concurrent with the growing acceptance of this approach, there has been a significant public and private effort directed toward health promotion and disease prevention--and growing evidence of effectiveness. Several recent publications have documented improvements in the Nation's health over recent years, as well as gains that may continue. Among these improvements are:

- The proportion of adults who smoke has declined by more than 20 percent over the past 15 years.
- The proportion of the population with high serum cholesterol levels has declined by 12-22 percent.
- The proportion of adults who exercise regularly has increased by as much as 100 percent. (USDHHS 1982)

Applied to alcohol-related problems, the public health approach directs simultaneous attention to (1) individuals at risk for developing problems, (2) the availability and distribution of alcohol, and (3) the drinking environment. Objectives of the Nation for 1990 include more than a dozen specifically related to alcohol (see box, page 124) and reflect attention to each of these three areas.

The Alcohol, Drug Abuse, and Mental Health Administration (1981) has defined primary prevention as actions or interventions designed to reduce the incidence of alcohol disorders and related problems. (Secondary prevention, or intervention, is concerned with the early identification and treatment of these disorders, to reduce their prevalence or the prevalence of dysfunctional behaviors associated with them.)

In 1981, the National Academy of Sciences completed a study (under contract to NIAAA) of alternative approaches to the prevention of alcohol-related problems. Based on this study, the Academy concluded that: The possibilities for reducing the (alcohol) problem are modest but real and should increase with experience (Moore and Gerstein 1981). This section of the chapter will set forth findings of research on two major instruments for preventing alcohol-related problems: (1) education, information, and training and (2) law and regulation.

Education, Information, and Training

School-Based Alcohol Education Programs

Alcohol education programs for youths 18 years of age and younger have focused on both general unselected youth populations and those at risk for alcohol problems (Hewitt 1982). Alcohol education programs for the former have ranged from those delivering only alcohol-related information to those with little or no alcohol-related content, and those designed to foster the personal development of participants to reduce the likelihood of later alcohol problems. Several programs have combined alcohol-specific education with personal development (NIAAA 1979, 1981b).

Educational efforts also have been directed at groups of adults who interact with young people and who are in a position to influence their drinking (Hewitt 1982). Programs for parents and other family members, teachers, other community professionals, and lay people have been developed, on the assumption that providing these key "gatekeepers" with information on alcohol and alcoholism may well affect the youth for whom they are responsible.

Evaluations of alcohol education programs indicate that: (1) significant increases in knowledge about alcohol are often observed (Fullerton 1979; Staulcup et al. 1979; Wittman 1982); (2) less dramatic but nonetheless real changes in attitudes toward alcohol or toward self and others also occur, especially when attitude change is an explicit goal of the program (Evans et al. 1979; Weisheit et al. 1979; Wittman 1982); (3) difficult-to-interpret or modest changes in actual drinking behavior occur, although fewer programs set out to measure behavioral change than changes in attitudes toward or knowledge about alcohol (Fullerton 1979; Staulcup et al. 1979; Wittman 1982); and (4) although evaluation designs are becoming more sophisticated, future studies will need to develop measurable and precise program objectives and goals (Wittman 1982).

Elementary-age children.--This group of children has recently become the focus of in-

1990 Objectives
Alcohol Abuse and Alcoholism

1. By 1990, fatalities from motor vehicle accidents involving drivers with blood alcohol levels of .10 percent or more should be reduced to fewer than 9.5 per 100,000 population per year. (In 1977, there were 11.5 per 100,000 population.)

2. By 1990, fatalities from other (non-motor-vehicle accidents, indirectly attributable to alcohol use, e.g., falls, fires, drownings, ski mobile, aircraft) should be reduced to 5 per 100,000 population per year. (In 1975, there were 7 per 100,000 population.)

3. By 1990, the cirrhosis mortality rate should be reduced to 12 per 100,000 population. (In 1978, the rate was 13.8 per 100,000 population.)

4. By 1990, the incidence of infants born with fetal alcohol syndrome should be reduced by 25 percent. (In 1977, the rate was 1 per 2,000 deaths, or approximately 1,650 cases.)

5. By 1990, per capita consumption of alcohol should not exceed the current levels. (In 1978, about 2.82 gallons of absolute alcohol were consumed per year per person aged 14 and over.)

6. By 1990, the proportion of adolescents 12 to 17 years old who abstain from using alcohol (or other drugs) should not fall below 1977 levels. (In 1977, the proportion of abstainers was 46 percent for alcohol.)

7. By 1990, the proportion of adolescents 12 to 17 years old who report acute drinking-related problems during the previous year should be reduced to below 17 percent. (In 1978, it was estimated to be 19 percent based on 1974 data.)

8. By 1990, the proportion of problem drinkers among all adults aged 18 and over should be reduced to 8 percent. (In 1979, it was about 10 percent.)

9. By 1990, the proportion of women of childbearing age aware of risks associated with pregnancy and drinking--in particular, the fetal alcohol syndrome--should be greater than 90 percent. (In 1979, it was 73 percent.)

10. By 1990, the proportion of adults who are aware of the added risk of head and neck cancer for By 1990, the proportion of adults who are aware of the added risk of head and neck cancer for people with excessive alcohol consumption should exceed 75 percent. (No baseline data are available.)

11. By 1990, 80 percent of high school seniors should state they perceive great risk associated with alcohol intoxication. (In 1979, only 35 percent perceived "great risk" associated with having five or more drinks per occasion once or twice each weekend.)

12. By 1990, the proportion of workers in major firms whose employers provide a substance abuse prevention and referral program (employee assistance program) should be greater than 70 percent. (In 1976, 50 percent of a sample of the Fortune 500 firms offered some type of employee assistance program.)

13. By 1990, a comprehensive data capability should be established to monitor and evaluate the status and impact of misuse of alcohol (and drugs) on: health status, motor vehicle accidents, accidental injuries in addition to those from motor vehicles, interpersonal aggression and violence, sexual assault, vandalism and property damage, pregnancy outcomes, and emotional and physical development of infants and children.

NOTE: Acute drinking-related problems have been defined as problems such as episodes of drunkenness, driving while intoxicated, or drinking-related problems with alcohol authorities.

creased prevention activities. Bartlett's (1981) analysis of alcohol education programs and their impact on elementary and high school age youth cautions against overemphasizing cognitive learning and lecture-oriented teaching methods, failing to assist students' receptivity to the material and to appreciate the problems caused by the "captive population" syndrome, and overlooking the importance of coordinating alcohol education programs with related community resources. Nontraditional programs that involve students in curriculum design and interactive learning seem most successful.

One innovative prevention approach to grade-school children--the Alpha Center Prevention Model--is in place in two Florida counties (Pringle et al. 1981). This model is based on the assumption that alcohol abuse, like other behavioral problems, derives from early developmental problems. Students aged 8 to 12 who display maladaptive behaviors at home and school attend special classes to improve social and academic skills. Their teachers learn classroom behavior management techniques and interpersonal communication skills, and a counselor works with parents at home. The Alpha Center concept remains essentially unproven, however.

Adolescents.--Most youth begin to drink in adolescence. This is also the time when youth are most at risk for the most catastrophic consequences of drinking: alcohol-related traffic accidents.

A recent study on adolescent alcohol abuse relevant to prevention efforts found that (1) alcohol is the most widely used drug by youth between the ages of 12 and 17 (making this group an obvious prevention target), (2) problem drinking increases sharply with advancing age during adolescence, (3) adolescent problem drinkers use illicit drugs much more often than nondrinkers, (4) heavy drinking during adolescence is typically accompanied by other antisocial behaviors, (5) both parental and peer influences strongly affect problem drinking, and (6) adolescent problem drinkers differ from non-problem-drinking adolescents--they are more tolerant of deviance, less successful in school, and prize more highly independence than academic success (Braucht 1982). Research on self-reported drug usage and problem behaviors indicates significant associations between such behaviors and use of alcohol, tobacco, illicit drugs, painkillers (e.g., aspirin), and tea or coffee (Hundleby et al. 1982). These findings emphasize the complex phenomena that prevention programs for youth should address, as well as the special characteristics and changing needs of the adolescent problem drinker.

The CASPAR program in Somerville, Massachusetts, took this complexity into consideration when it included teacher training, peer teaching programs, and an alcohol-specific curriculum to teach decisionmaking, problem solving, and coping skills. It found substantial increases in knowledge and improved attitudes. The peer leadership training was found effective in raising levels of self-esteem, feelings toward home environment, and optimism. A significant inverse relationship was found between levels of self-esteem and likelihood of problem drinking (NIAAA 1979). Changes in drinking behavior did occur in the experimental group as compared with the control group, which was not exposed to the program over a period of 3 years (Wittman 1982). These effects decayed when junior high youth moved into the high school, however. The experimental group showed as high a level for alcohol-related problems as did the control group in high school (NIAAA 1979).

The Here's Looking At You curriculum program in Seattle, Washington, found similar results with a multifaceted program that paid particular attention to the alcohol discussion content of the curriculum in relation to the developmental age of the child. The most encouraging of the findings was that for the age cohort sixth-eighth grade (the longitudinal subsample first measured while they were in sixth grade and then during the succeeding 2 years), the impact from the curriculum was found not only in knowledge, but also in increasing self-esteem and, in some, improving decisionmaking skills (NIAAA 1981b). Further study of this curriculum is expected to yield more knowledge about the impact of the curriculum on intervening variables and actual behavioral outcomes.

One program for high-risk youth at the high school level has proven effective in terms of behavioral change. The Student Assistance Program, implemented in 23 schools in Westchester County, New York, has a primary prevention component aimed at newcomers, seniors, children of alcoholics, and young people with interpersonal problems. Using small groups facilitated by a trained counselor, the program has proven effective in reducing the incidence of both alcohol problems and absenteeism (often associated with alcohol and other drug problems) (NIAAA 1983).

Another innovative program focusing on a high-risk group of delinquent adolescents included an intensive training program for the staff of the Partners Program, a nonprofit volunteer organization designed to provide services to youths in trouble with the law in Denver, Colorado (Resource Alternatives Corp. 1982). Another essential component of the program was peer education. The program's evaluation study design provided for three control groups, all of whom were enrolled in the program before the alcohol education/prevention training component was provided to the staff. Results of the evaluation revealed that youths' perceptions of the negative consequences of drug and alcohol use increased after their counselors had been exposed to alcohol education. More important, the experimental groups experienced less severe alcohol and other drug problems than did the control group (NIAAA 1981a).

A project conducted jointly by the American Medical Association and the American Association of Motor Vehicle Administrators (Hames and Petrucelli 1980) was based on the assumption that teenagers in the process of getting their driver's licenses are maximally motivated to cooperate with an alcohol education program attached to that process. The program required teenagers applying for license in New York, Wisconsin, or Oklahoma to view an alcohol education film in high school driver education classes, after which they were tested for knowledge increase and retention. Results indicated that the information was retained at least for a short time; however, the impact of the program on subsequent rates of drunken driving was not assessed.

One of the most thorough studies of the impact of alcohol education on adolescents (Stuart 1980) included lectures given to almost 1,000 junior and senior high school students on the physiology and pharmacology of drugs including alcohol and the legal, social, and psychological ramifications of their use. While information levels increased, drug and alcohol use also increased.

A study by Goodstadt and his colleagues (1982) found that educating 7th to 10th grade students on myths about alcohol, beverage advertising, reasons for drinking, and effects of alcohol on the family, driving, sports, fitness, and sexuality improved their knowledge but had mixed effects on their attitudes toward alcohol. Moreover, during the program, the students decreased their alcohol consumption. Since this is one of the few adolescent alcohol education projects that assessed behavior change and clearly found evidence of change, it deserves careful scrutiny and possible replication.

Goodstadt and Sheppard (1983) also recently compared three short-term programs--a cognitive program, a decisionmaking program, and a values-clarification program--for high school students. The cognitive program improved levels of alcohol knowledge significantly more than the other programs, even though there was no change in behavioral expectations or attitudes. The decisionmaking program was successful in leading students to a better understanding of major decisionmaking concepts, demonstrating the viability of this program in teaching about decisionmaking. The values-clarification program was most likely not appropriate for the target audience, so no generalizations could be made.

The authors did draw, however, some significant conclusions. They found, for instance, that while attitudes were not changed by these programs, attitude change is positively related to reduced alcohol consumption. They also found that those who improved in their use of decisionmaking concepts were more likely to show a shift toward less pro-alcohol attitudes. They concluded that "whereas behavioral outcomes are a desirable objective, they probably represent unreasonable expectations for interventions of such short duration, although they would continue to be significant long-term objectives and worthy of examination" (Goodstadt and Sheppard 1983).

College-age youth.--An effort to stimulate prevention and intervention programs has been made at the college level in recognition of both the paucity of such programs to this time and the differences in approach and strategy required for effective prevention and intervention with this population (Bryan 1982; Dean 1982).

Several interesting approaches to prevention with college-age youth have been reported. A survey of 457 Memphis State University students and 30 mental health professionals working in the university setting revealed that the students, unlike the professionals, considered substance abuse problems to be the most serious of 24 mental health problems experienced by students (Henggeler et al. 1980). Evaluations of alcohol education programs at the University of Virginia (Portnoy 1980) and Saint Mary's College (Leavy 1980) both demonstrated the apparent ease with which the student's information, based on al-

cohol knowledge, can be changed--and the real difficulty in changing actual drinking behavior. Similar results were obtained at Brown University by a "sons and daughters of alcoholics" group designed as a prevention and intervention strategy (Donovan 1980).

Between 1975 and 1980, a comprehensive alcohol education program for college students was developed, implemented, and evaluated at the University of Massachusetts (Kraft 1982) and somewhat later replicated and extended at the University of North Carolina (McCartney and Humbert 1983; Mills et al. 1983). These two projects were among the most carefully evaluated of all large-scale prevention projects directed at this population of drinkers. The University of Massachusetts project programed mass media messages to raise awareness of drinking and driving, and sponsored group discussions and community development techniques designed to influence ways in which alcohol was consumed by college students. As a result of these efforts, knowledge and attitude changes took place; however, no positive changes in drinking behavior were observed (Kraft 1982). The evaluation design, however, was invalidated, since during the program the minimum purchase age was lowered in Massachusetts. It is impossible to know, therefore, if behavioral changes occurred as a result of the program.

Mass Media Campaigns

The consensus about mass media information campaigns is that: (1) such efforts are largely limited to increasing knowledge and reinforcing established attitudes and behavior patterns (Blane and Hewitt 1977), and (2) slight alteration on changing drinking patterns may occur, although this effect is indeterminate (Blane 1976). However, Wallack (1981) notes that:

> A review on the effects of mass media would lead one to a healthy skepticism regarding the effectiveness of such a program implementation technique. This skepticism must be tempered because of the flawed evaluations which have generated the body of effectiveness data....It may be that determining the effects of mass media is a function of broadening research questions to gain better understanding of the wider view, rather than narrowing them further to assess individual exposure and reaction in greater detail (p. 230)

NIAAA's recent mass media campaign clearly indicates that such efforts can stimulate interest in both the prevention of alcohol problems and communitywide organization and development toward this end (NIAAA 1982).

Education Programs About Other Health Hazards

Recently, attention has been devoted to determining what can be learned about prevention of alcohol-related problems from carefully developed programs intended to reduce other health hazards (Hochheimer 1981). And some have concluded that the most promising prevention technique for the 1980s is the community-based model that blends a variety of approaches aimed at the host, agent, and environment to address the complexities and needs specific to the community (Hochheimer 1981; Wittman 1982; Holder and Blose 1983).

One design that combined mass media campaigns with intensive interpersonal training at the local level was the Stanford Heart Disease Prevention Three Community Study. This study had the following five goals: generate awareness about the program and its focus, increase the knowledge of the audience, motivate people to adopt new behaviors, teach people new skills, and reinforce the new skills and behaviors so they would be maintained (Hochheimer 1981). Their findings showed that dietary changes and exercise were learned through mass media alone (Maccoby and Farquhar 1975). However, other behaviors, such as smoking, changed only when interpersonal training (based on the social learning and behavior work of Bandura 1977, 1978, 1979, and Goodstadt 1978) was included (McAlister et al. 1979). After 2 years, the overall decrease in risk of heart disease was 16-18 percent in the experimental sites, compared with 6.5 percent for the control group.

In Project CLASP (Counseling Leadership About Smoking Pressures), which was based on previous smoking and health research, McAlister and colleagues (1979) trained several teams of five to seven high school students to lead classroom sessions for junior high school students. The objective of the sessions was to increase students' commitment not to start smoking and to psychologically "inoculate" them against pressures to smoke. Similar activities aimed at deterring the use of alcohol and other drugs also were added. When the experimental and control schools were compared following 21 months of longitudinal ob-

servation, the experimental school's students were found to be smoking and drinking significantly less than students in the control school, who had received an intensive course in health education but no peer-group sessions with high school students. Further evaluation is needed to see if this effect persists over time and to gain a better understanding of these efforts.

Other prevention programs based on social learning theory (Bandura 1977) emphasize strategies encouraging young people to refuse drugs. Significant positive results have been found in university-based research and demonstration programs aimed primarily at smoking prevention. Other research has supported the assumption that rehearsing responses to detrimental health influences increases the likelihood that these responses will be used in appropriate situations (McGuire 1969).

Most refusal programs incorporate three components: strategies that increase young people's knowledge by providing information about both the hazards of drugs and their effects, and about peer pressure and other influences to use drugs; techniques for expanding one's specific behavior repertoire for saying "no"; and training in life skills (e.g., values clarification, enhancing self-esteem, assertiveness training, problem solving, and coping abilities). As a wide body of research has shown, each plays a part in a person's choice to adopt either life-enhancing or health-risking behaviors (Bandura 1969; Rotter 1972; Jessor and Jessor 1977; Perry 1981).

In one such program--Project SMART at the University of Southern California--the principal objective has been to implement and study a school-based prevention program designed to offset peer pressure through the use of positive strategies to refuse drugs and thereby reduce cigarette smoking and alcohol and marijuana use in the sixth through ninth grades. In Project SMART, two curriculums have been developed; one focuses on social resistance skills training, and the other stresses self-management skills and values clarification. Both use peer leaders. Pretest findings indicate that it may be important to begin the intervention at a point where the target audience begins to perceive itself at risk, and that youth prevention programs are more effective when facilitated by peers (Johnson et al. 1981).

In the Life Skills Training Program, a similar program developed at the Cornell University Medical School, students are informed about myths and realities relating to smoking. In addition, they are assisted in improving self-image, making informed choices, and resisting pressure to smoke. Advertising techniques, verbal and nonverbal communication skills, and appropriate and effective use of assertiveness also are examined. The material in each of these sessions is transmitted through discussion, demonstration, and role playing, and often is not smoking-specific, although connections are made where appropriate. Students also participate in a self-improvement program in which they identify a skill they want to improve or a behavior they want to change and then set long- and short-range goals for accomplishing this. Botvin and Eng (1982) have found that the program increased knowledge and reduced by 58 percent the onset rate of smoking. In addition, the experimental group expressed less social anxiety and were more resistant to influences than the control group.

Wellness programs may offer additional opportunities for alcoholism prevention at the worksite. Wellness programs--positive lifestyle change programs--offer healthy employees the opportunity to modify lifestyles that might, at a future date, cause health problems. Smoking cessation, exercise, stress management, weight control, and nutrition programs are typically offered in the effort to promote healthier lifestyles, improve quality of life at present, and reduce health risks in the future. A number of large corporations, including Johnson & Johnson and Control Data, have put wellness programs into place. These programs may, but typically do not, provide alcohol components, relying instead on existing employee assistance programs (EAP) to reach employees with alcohol problems. When no EAP exists to address stigmatized problems, its inclusion may greatly enhance the company's human wellness program. However, the existence of comprehensive positive lifestyle change programs may affect drinking practices and general awareness of healthy lifestyles, thereby preventing alcohol problems from developing in some individuals. Empirical studies of the impact of these programs on the prevention of alcohol problems are necessary before their role and widespread implementation in the worksite can be determined.

Programs for Populations at Special Risk

Women.--In the past, few prevention approaches have been designed specifically for women. These usually provided assertiveness training, exercises for enhancing self-esteem,

and stress management seminars (Irwin 1976; Sandmaier 1976). To date, neither the underlying assumptions nor the program effectiveness of these types of programs have been confirmed empirically.

One program currently being evaluated is the Alcoholism Center for Women, Los Angeles County, which recently developed a systematic community approach for identifying and delivering prevention activities to adult women at high risk for alcohol problems. Special attention was paid to developing a method to identify populations of high-risk women and their psychological and sociological predisposition to alcohol abuse. Using this information, the Alcoholism Center designed and implemented a multimedia, multifaceted prevention strategy, which is being tested.

Minorities.--For many years, accurate data on the nature and extent of alcoholism among ethnic and racial minorities within this country were unavailable, making the task of targeting prevention efforts within and between these groups difficult. Now, however, better data are available on alcoholism and problem drinking among black, Asian, Hispanic, and Native Americans. An important issue related to understanding variations among ethnic groups in use of alcohol and incidence of alcohol problems has been whether these variations derive more from sociocultural, biochemical, or physiological differences. Although current data attribute predominant influence to sociocultural differences (Schaefer 1982), the determination of significant genetic contributions to alcoholism risk indicates the need to more fully examine biochemical and physiological parameters. Thus, a final answer to the question awaits more sensitive bioassay methods and more sophisticated sociocultural survey designs.

While drinking behavior of youth and the elderly in the black community remains largely undocumented, the findings from a few prevention programs for black youth (Crisp 1980; Miranda 1981) and black women (Gaines 1976) have been reported. Such projects need to be studied in depth to empirically assess their effectiveness. Of particular concern for prevention programers is the fact that young black males (aged 25-34) in metropolitan areas are as much as 10 times more likely than young white males of the same age to die from cirrhosis of the liver. This disproportionately increased rate remains higher for black males until age 65 (Malin et al. 1982). In addition, although it appears that blacks drink less than whites, when they drink they drink more heavily, thus increasing the likelihood of certain negative consequences associated with heavy drinking (Roizen 1982).

Rates of alcoholism among Hispanic Americans appear to be higher than the national average (Garza 1979). Variables that may explain these elevated rates of alcohol abuse include sociocultural norms and values that encourage heavy drinking, especially by men, minority group status, problems of acculturation and their associated stresses, and possible biochemical and physiological factors. Causal relationship between these factors, singly or together, and alcoholism, in either individuals or groups of individuals, has to this time only been inferred. Hispanic Americans, like other minority groups, underutilize treatment and rehabilitation resources, and few prevention programs have been designed for them (Alcocer 1982).

Elderly persons.--Strong evidence exists that the percentage of drinkers begins to decline at age 50, and at age 60 to 65, the percentage of heavy drinkers among males drops even more sharply. From age 50 on, however, some older people who have been lifelong abstainers or moderate social drinkers become problem drinkers (NASADAD 1981; Brody 1982). But the negative attitudes of many mental health professionals toward older persons seeking help make the prevention and treatment of alcoholism in the elderly very difficult. One solution may be support for self-help groups--older persons helping those in need--as well as a greater emphasis on preretirement planning that may affect use and abuse of alcohol (Gomberg 1982). Loss, such as that reflected in retirement, appears to be an impetus for developing alcohol problems in this age group. In addition, isolation is of particular significance for prevention programers, e.g., how to reach the large numbers of women in this age group who have experienced loss and who are living alone.

An assessment model to help plan treatment and prevention services for the elderly has been proposed (Kola and Kosberg 1981). Designed to consider the special needs of the elderly for prevention and treatment services, the model recognizes the importance of integrating these services into existing community treatment and prevention resources. An example of a self-help program effectively integrated into its community is located at the Eagleville Hospital and Rehabilitation Center, where it began drug and alcohol prevention

services to the elderly in Montgomery County, Pennsylvania, in 1978 (Leigh 1980).

Infants.--Alcohol consumption during pregnancy poses a significant risk for the unborn child, with consequences including increased spontaneous abortion, decreased birth weight, major and minor birth defects, and mental retardation.

These effects of alcohol on the developing human fetus are detailed elsewhere in this volume (see chapter 5). Some occur in children whose mothers, during pregnancy, consume alcohol in amounts consistent with a diagnosis of alcoholism. Some occur in children whose mothers drink moderately. All of them are completely preventable.

A variety of prevention approaches will be necessary to reach social or moderate drinking women and women who drink heavily. The Surgeon General's health advisory on the risks of alcohol consumption during pregnancy, issued in July 1981 (FDA), pointed up the need to prevent alcohol-derived birth defects. This advisory urged physicians and other health professionals to advise patients who are pregnant or considering pregnancy not to drink alcoholic beverages.

One of the best documented fetal alcohol syndrome (FAS) prevention programs is the Fetal Alcohol Syndrome Demonstration Program at the University of Washington (Little et al. 1980; McIntyre 1980). This program aimed at providing model public and professional education on FAS, clinical services for pregnant women, assessment services for FAS children, and ongoing evaluations of these activities. Compared with a control community, there was a significant increase in the number of women who agreed to become abstinent during pregnancy. However, the program was less successful in reaching the pregnant "excessive drinker" who was drinking at levels reported to pose a risk to the fetus. Thus, it may be indicated that some women who are exposed to programs on alcohol and pregnancy will decrease their drinking, while other women who drink more heavily may require specialized services such as those offered by the obstetrical community in terms of screening techniques for early intervention and subsequent referral for treatment (Little in press).

Other efforts--one in Goteborg, Sweden, and one in Boston--have reported highly successful outcomes utilizing a secondary prevention approach (Olegard et al. 1979; Rosett et al. 1980, 1983). During their first prenatal visit to an obstetric clinic, women fill out a structured health history that elicits information on alcohol use as well as other items. Women who reported consuming more than 45 drinks per month were counseled in a nonconfrontative manner about the benefits of decreasing alcohol consumption for having healthier babies. Fetal outcomes were markedly superior for those heavy drinking women who decreased alcohol consumption or abstained during the remainder of the pregnancy to those for heavy drinkers who did not change their drinking behavior. Of particular interest, the Boston study tentatively concluded that either the later pregnancy period is most crucial for alcohol teratogenicity, or reversibility of injury is possible if heavy drinking is terminated early enough during the pregnancy course. Further work may clarify exactly when prevention efforts can be implemented for optimal effectiveness.

A recent cross-sectional study compared drinking patterns during pregnancy over a 6-year interval (Streissguth et al. 1983). Different samples of pregnant women were interviewed in 1974 and 1975 and in 1980 and 1981. In the interim period, the study population was exposed to public media and educational programs on alcohol and pregnancy. Although the proportion of women drinking during pregnancy was found to have decreased during the 6-year interval, the proportion of women drinking at least an ounce of absolute alcohol per day was relatively constant. Since it is precisely this limited proportion of the population that incurs the highest risk of alcohol-related birth defects, these results highlight the need for more intensive prevention efforts.

Law and Regulation

Since the publication of the Fourth Special Report to Congress (USDHHS 1981), a number of studies have been published, exploring the implications of legislative and regulatory approaches for the prevention of alcohol-related problems. The findings of these studies are summarized here.

International Studies

In collaboration with the World Health Organization (WHO), the International Study of

Alcohol Control Experiences (ISACE) reviewed historical patterns of alcohol consumption, problems, policies, and their effects in Finland, Ireland, the Netherlands, Canada, Poland, Switzerland, and the United States (specifically, California).

The study, entitled Alcohol, Society and the State (Makela et al. 1981), found that "growth in alcohol consumption was accompanied by an increase in a broad variety of problems related to drinking....This holds not only for consequences of prolonged drinking, but for social and health problems related to single drinking episodes as well." Noting that "from a policy perspective it is perfectly legitimate to be interested in the autonomous impact of alcohol control on consumption and problems," the authors state that "from a historical perspective, the notion of effect is problematic.... Most of the time, changes in policy measures have, in fact, been one facet of the same general social processes, and changes in consumption, another." (p. 109)

The report also concluded that (1) "a reorganization of responsibilities among branches of government may be required to achieve a successful combination of economic, health, and social considerations;" (2) "preventive alcohol policies should...be given a high priority as an alternative to the morally inspired control of problem drinkers;" (3) "policy changes on alcohol should be made with caution and a sense of experiment;" (4) "while control of availability should receive a high priority, it is important to consider governmental powers to manipulate the environment of drinking so as to lower the risk of adverse consequences" (e.g., traffic fatalities and alcohol-related violence); (5) "international organizations should give close attention to existing and future trade policies and arrangements with a potential for affecting the availability of alcoholic beverages" (Makela et al. 1981, pp.110-112).

In June 1982, the National Academy of Sciences published the proceedings of an Institute of Medicine (IOM)-supported inter-American workshop entitled Legislative Approaches to Prevention of Alcohol-Related Problems. The purpose of this workshop was to explore the issue of economic growth, alcoholism, and alcohol-related problems by reviewing available data and the experiences of other countries to help policymakers in the Americas understand the complexities governing public policy decisions. The consensus emerging from the conference participants was that: (1) the cost to society from episodic alcohol intoxication in the Americas is the most neglected alcohol issue; (2) increased interest in group-oriented measures aimed at preventing alcohol-related problems should be developed; (3) available empirical evidence suggests that a number of prevention-oriented, legislatively based policies should integrate public health and economic development benefits and costs with the social, cultural, and political societal values; (4) public and governmental awareness must precede implementation of effective policies; and (5) while the experiences of one country can assist others, a country's alcohol-related prevention strategies must be shaped by its own unique social, cultural, political, and economic situations (Institute of Medicine 1982).

The ANSVAR Mutual Insurance Company, in connection with the 1981 annual conference of the International Council on Alcohol Addictions, published Alcohol in the World of the 80's: Habits, Attitudes, Prevention Policies and Voluntary Efforts (Armyr et al. 1982). This broad inquiry detailed conditions in 23 countries or groups of countries with respect to drinking habits, alcohol control policy, economic issues, and efforts from the voluntary sector. This review concurred with the findings of ISACE and also concluded that, in the coming 5 years, alcohol consumption was more likely to increase than decrease, along with many indicators of alcohol-related problems.

Taxation

As the ISACE study noted, there is a "relatively large econometric literature on the relation of alcohol taxes and prices to consumption" (Makela et al. 1981, p. 89). Recent studies attempt to address more clearly the relationship of alcohol taxes to alcohol-related problems.

In particular, Cook and Tauchen (1982) estimate that an increase in the liquor excise tax by $1 (1967 prices) per proof gallon (viz., 64 ounces of ethanol) would reduce the liver cirrhosis mortality rate by 5.4 percent in the short run and perhaps by twice that amount in the long run. Cook also offers a historical example: When France imposed stringent wine rationing in 1942, the cirrhosis mortality rate in Paris fell from 35/100,000 in 1941 to 6/100,000 in 1945-46, only to return to its previous higher levels when rationing ceased in 1948. Other work (Mello 1972; Nathan and Lisman 1976) offers clinical evidence that

alcoholic persons do reduce their alcohol consumption as a function of the beverage costs.

Cook (1981) also found that increases in the tax rate of spirits will reduce both the auto fatality rate and the cirrhosis rate. Smith (1981) draws the same conclusion. Two reviews of these relationships worldwide (WHO 1979; Colon 1980) suggest that while alcoholic beverages behave as other market commodities do (in that consumption is affected by price), there are also complicated interactions between the availability of alcohol supplied by the distribution network and the pricing of alcohol.

Cook and Tauchen (1981) also note that the Federal tax on alcoholic beverages has remained constant in nominal terms since 1951. Thus, the real price of alcoholic beverages has actually declined in recent years, such that between 1960 and 1980 the real price of liquor declined 48 percent, beer 27 percent, and wine 20 percent.

On balance, the weight of opinion (Cook 1981) appears to be that consumption is affected by price, and data exist in support of this view. Moreover, the previously held view that reducing overall consumption does not affect consumption by the heaviest drinkers (Makela 1975) is being challenged and reevaluated (Makela 1980; Smart 1982). Many countries already have adopted the view that increasing the price of alcoholic beverages is a viable control strategy. Sweden (Somervuori 1977), Finland (Koski 1977), Australia (Luey 1979), Poland (Malec 1980), and some European Common Market countries (Sulkunen 1978) employ some form of price policy as a consumption control.

Minimum Drinking Age

There is considerable evidence that increasing the legal age for possession, purchase, consumption, or sale of alcoholic beverages can be an effective measure to reduce drunk driving accidents among youth (Douglass et al. 1974; Wagenaar 1980; Wagenaar et al. 1981; Maxwell 1981; Williams et al. 1983; Hingson et al. 1983). A study by Wagenaar (1980) analyzed a random sample of 20 percent of all reported accidents (i.e., fatal, injury, and property damage) in Michigan from January 1972 to December 1979. It concluded that:

> Controlling for trends, seasonally, and other patterns in the frequency of police-reported 'had been drinking' (HBD) crash involvement among 18-20-year-old drivers, an [annual] reduction of 31 percent occurred in the first 12 months after the drinking age was raised from 18 to 21 in December of 1978. Analyses of late-night, single-vehicle crashes with a male driver, of which a majority have been consistently identified as involving a drinking driver, reveal a significant reduction of 18 percent among drivers aged 18-20 after the higher legal drinking age was implemented. (Wagenaar 1980, p. 148)

In another study (Maxwell 1981), made after Illinois raised its minimum legal drinking age in January 1980 from 19 to 21 years, data for single-vehicle, nighttime, male-driver involvements occurring between 8 p.m. and 3 a.m. were used as a surrogate for alcohol-involved accidents. This study, comparing 1980 with 1979 accident data, concluded that raising the legal drinking age law was effective in reducing the single-vehicle, nighttime, male-driver involvement for drivers aged 19 and 20. For 1980, the percentage of reduction attributable to the law change was 8.8 percent.

The Michigan and Illinois studies looked at all accidents--fatal, injury, and property damage. Another study (Williams et al. 1983), using data from the Fatal Accidents Records System (FARS) of the National Highway Traffic Safety Administration, looked at nine States that raised their legal minimum age. Eight of the nine States experienced a reduction in nighttime fatal crash involvement among drivers in the affected age group; the average annual reduction was 28 percent. A recent study (Wagenaar et al. 1981) on the effects of raising the minimum age in Michigan and Maine concluded that Michigan drivers aged 18-20 experienced a net reduction of approximately 20 percent in the frequency of involvement in alcohol-related injury-producing crashes due to a raised drinking age from 18 to 21; in Michigan, there was a 17-percent decrease in alcohol-related crashes damaging property for the same age group; and in Maine, 18- to 19-year-olds were involved in 20 percent fewer alcohol-related crashes damaging property.

There also is evidence that contiguous States with differential minimum drinking ages create problems with cross-border purchase of alcohol by youth (Lillis et al. 1982). Based on these studies, the National Transportation Safety Board recommended in 1982 that all States raise the minimum legal age for

drinking or purchasing all alcoholic beverages to 21. Several States have done so, and many introduced this kind of legislation in 1982 and 1983.

Highway Safety

In seeking to reduce injuries and fatalities from alcohol and highway traffic accidents, the legislative area has received increased attention. New laws are mandating stringent minimum penalties for intoxicated driving offenders and supporting more intensive enforcement of existing intoxicated driving laws. These legislative approaches are being taken to establish new limits on driving and drinking and to decrease the incidence of driving while intoxicated.

A recent review of intoxicated driving literature (Borkenstein 1981) suggested that the role of alcohol in traffic accidents can be curtailed by (1) reducing per capita alcohol consumption (by increasing price or raising drinking age); (2) constructing streets and highways that place fewer demands on drivers so the effects of alcohol are not as severe; and (3) increasing enforcement to bring about general deterrence of drinking and driving.

In Survey and Deterrence of the Drinking Driver: An International Survey, Ross (1981) reviewed the experience of various countries in adopting the Scandinavian model, which combines the principles of deterrence with laws related to drinking and driving. He concludes that "enactment and enforcement of drunk driving laws are most successful in their initial deterrence of drinking and driving. When certainty of punishment for drinking and driving violations is low, however, this initial deterrent effect disappears. A reasonable interpretation of the results of this review is that Scandinavian-type laws deter when initiated because of exaggerated perceptions of the risk of apprehension and punishment. Since they appear to increase the real risks much more moderately, the deterrent accomplishment rests not on a firm foundation, but rather on a temporary scaffold that becomes undermined through experience." Furthermore, Ross suggests that "research is needed to determine the function of the components of legal threat in affecting the behavior of drinking and driving, particularly the relation between actual and perceived certainty, severity, and celerity of punishment (Gibbs 1975); and the interaction between certainty and severity of punishment."

Current Activities

World Health Organization

In 1979, the World Health Assembly recognized that problems related to alcohol--excessive consumption, in particular--rank among the world's major health problems. A resolution was passed urging the member States to take all appropriate measures to deal with the increasing problem and requesting the director general to strengthen the World Health Organization's (WHO) capacity to this end (WHO 1979, 1980).

At the 1982 World Health Assembly, technical discussions involving 300 delegates from 100 countries were held on the topic "Alcohol Consumption and Alcohol-Related Problems: Development of National Policies and Programs." The need for national alcohol policies to overcome future problems was accepted by every discussion group, as was the need to mobilize "political will" to overcome the inevitable difficulties in developing national alcohol policies. Furthermore, this political will must spring from the grassroots and should represent the community as well as the Nation. A major recommendation emanating from these discussions was that alcohol-related problems be given their vitally important place in all strategies for reaching the goal of "Health for All by the Year 2000."

In 1983, the World Health Assembly passed a resolution reiterating the firm conviction that problems relating to alcohol consumption rank among the world's major public health concerns and constitute a serious hazard for human welfare. This resolution recommended that member States formulate explicit and comprehensive national alcohol policies with prevention as a priority within the framework of the strategy of "Health for All by the Year 2000." The resolution also asked WHO not only to continue but to intensify its program on alcohol-related problems as an integral part of the strategy and to strengthen its capacity to respond to requests from member States to support their efforts in dealing with alcohol-related problems.

National

Health promotion.--To achieve the 1990 health objectives, many agencies within the Department of Health and Human Services (DHHS) are increasing their collaborative activities. For example, the National Cancer Institute and NIAAA are in the process of de-

termining the appropriateness of and strategies for a public education effort designed to raise awareness about risks of alcohol-related cancers.

Furthermore, specific DHHS agencies are working with the Department of Defense (DOD) to introduce a comprehensive health promotion effort that includes preventing alcohol abuse and alcoholism within the military, as well as with DOD developers of a curriculum guide for use in dependent schools overseas.

Youth.--In 1982, the Secretary of DHHS undertook an Initiative on Teenage Alcohol Abuse to address the risks associated with the consumption of alcohol by youth. This effort, which was supported by the Departments of Transportation (DOT) and Education (DOE), included dissemination of model programs, joint initiatives with the private sector, regional prevention and treatment conferences, and a national conference held in Washington, D.C., designed to draw national attention to the work of a growing number of youth-directed drinking and driving programs. The Initiative will be continued through efforts directed at youth at high risk for development of alcohol problems.

In addition, DHHS and DOE are collaborating to explore the role of schools in preventing adolescent health problems. The Adolescent School Health Promotion Demonstration Program will focus on ways to improve the integration of alcohol, drug abuse, and mental and general health promotion/prevention principles into school management policies, health services, and curriculums.

Highway safety.--Subsequent to the initiatives of grassroots movements at the local and State levels, e.g., Mothers Against Drunk Drivers (MADD), Students Against Drunk Driving (SADD), Remove Intoxicated Drivers (RID), PARK IT, and Citizens for Safe Drivers, a number of activities have taken place at the national level. The Presidential Commission on Drunk Driving was created in April 1982 to heighten public awareness of the seriousness of the drunk driving problem, persuade States and communities to strengthen their law enforcement and trial process, and encourage State and local officials to accept and use the latest techniques and methods to solve the problems and to generate support for increased law enforcement. The Commission's final report will be completed by the end of 1983. Recently, the National Safety Council developed a plan of action addressing this problem. The Council's program, consisting of six measures, including public education, is intended to continue the national momentum against intoxicated driving.

The Alcohol Traffic Safety and National Registration Act of 1982 (Public Law 97-364) authorizes incentive grants to the States to encourage the establishment of effective alcohol safety programs. Administered by the National Highway Traffic Safety Administration (NHTSA), the law provides a basic grant to States that meet a minimum set of standards and a supplemental grant when additional provisions are incorporated. National Drugged and Drunk Driving Awareness Week, also enacted by Congress, stimulated a sense of national priority about this problem during the week of December 12-19, 1982.

Within the Federal Government, several agencies and departments have joined to increase efforts to reduce alcohol-related highway accidents. For instance, NIAAA and NHTSA and the Department of Defense have strengthened interagency collaboration to prevent such accidents. NHTSA's approach vigorously supports a six-step countermeasure model.

Policy conference.--As noted earlier, in 1981, the National Academy of Sciences published a report on its study of alternative approaches to prevention to alcohol-related problems (Alcohol and Public Policy: Beyond the Shadow of Prohibition). In May 1983, under contract to NIAAA, NAS convened a cross section of national, State, and local leaders to examine the study's conclusions and to distill ideas for future research and effective prevention measures. Discussions centered on the supply of alcohol, communicating about alcohol, and community cooperation to reduce alcohol problems. The participants--representing Government, business, State legislatures, public interest organizations, and the scientific community--agreed that a "network of policies" and not a single-focus strategy could be effective in reducing alcohol-related problems. The proceedings of this conference will be published in late 1983.

State and Local

The Omnibus Budget Reconciliation Act of 1981 incorporated Federal resources for alcohol-related prevention and treatment services into the Alcohol and Drug Abuse and Mental Health Services Block Grant. Of the

amount used in any fiscal year for alcohol or drug abuse activities, the States must use not less than 20 percent for alcohol and other drug abuse prevention and early intervention. A report including information on services provided under this block grant will be submitted to Congress in January 1984.

Through the combined efforts of many State Alcohol Authorities and NIAAA, a public education campaign directed at women and youth was successfully implemented. It targeted alcohol problems among women, alcohol consumption during pregnancy, and alcohol problems among youth, including drinking and driving. Television, radio, and print materials were disseminated through a multilevel strategy designed to encourage both State and local collaboration and involvement from a wide consortium of groups interested in alcohol problems. The States provided resources for dissemination of the materials, organized the campaign efforts, and developed local programs. Furthermore, many States and local communities developed additional public service announcements and print materials.

Thousands of people became involved in this effort across the country, and process evaluation indicates that the campaign was cost-efficient and successful in reaching the target audiences. More than $10 million was donated by the private sector for airing of alcohol-related television public service announcements during the first 11 months of the 1982 campaign, at a cost of less than 1.1 cent per person. Twenty percent of the public service announcements were broadcast between the hours of 5:00 p.m. and 11:30 p.m., one of the prime viewing times for women and youth (NIAAA 1983).

A national prevention network, composed primarily of State prevention coordinators, has been formed as part of the National Association of State Alcohol and Drug Abuse Directors (NASADAD). This group represents an important prevention resource for the Nation. It is now formalizing organization and developing operating procedures and agendas (NASADAD 1983).

Many States are particularly aggressive in their pursuit of preventing drinking and driving accidents and fatalities. During the 1983 legislative session in the States, 378 separate pieces of legislation related to alcohol and/or drugs and highway safety were introduced in 37 States, and 38 laws were enacted (NASADAD 1983).

A number of States have been active in gathering data on the problem and then organizing and expanding programs for persons arrested for driving while intoxicated (DWI). Some States and local communities have found that organizing a task force on intoxicated driving can be instrumental in eliciting cooperation. For example, the Governor's Alcohol and Highway Safety Task Force in New York was co-chaired by the director of the Division of Alcoholism and Alcohol Abuse and the commissioner of the Department of Motor Vehicles. This task force established one goal: "to reduce dramatically the incidence and tragic consequences of drunk driving in New York State." To achieve this goal, a comprehensive systems approach was recommended. The task force's recommendations resulted in legislative changes, the most significant being user funding for DWI programs.

The State of South Carolina also has been especially active in the area of drunk driving through the appointment of four regional task forces that will use community-based involvement to work on reducing the growing problem of drinking and driving in the State. The State Government also has introduced a comprehensive legislative package that would raise the legal drinking age to 21, prohibit the possession of an open container of beer or wine in a moving vehicle, provide that a blood alcohol concentration of .10 percent or more is legal evidence of impairment, and require that offenders render services to their community (NASADAD 1983).

Other States--Michigan, California, Maryland, Maine, Vermont, and Massachusetts, for example--have implemented campaigns and programs within their communities. The year-end figures for 1982 showed that more than 5,000 fewer fatalities were recorded than in 1981. This also represents a 14-percent decrease since 1980 (NHTSA 1983). NHTSA recently selected 10 cities, counties, and States to undertake special efforts to remove intoxicated drivers from the highways. The 10 sites have been designated "targets of opportunities," a concept developed to promote the adoption of comprehensive, community-based, general deterrence alcohol programs. The results of this effort hold potential for future prevention of public health problems.

An important point made about State and local prevention programs is that there is a lag in prevention programing and prevention outcome. According to the CONSAD Research Report on Prevention (McCartney and Humbert 1978), prevention must involve a large enough population base, over time, to actually affect social norms. An example that proves

the point, the Cottage Meeting Program (Boswell 1983), found that after 10 years it had changed community norms and attitudes, resulting in an increased demand for prevention services.

Private Sector

In 1982, the National Council on Alcoholism (NCA), which pioneered the concept of alcoholism as a disease and a major health problem, adopted a position paper on prevention (NCA 1982; Tofany 1983). This paper expresses NCA support for a wide variety of approaches, including education, information programs, regulatory measures including advertising curbs, an increase in Federal excise taxes on alcoholic beverages, a nationwide legal drinking age of 21, and a series of rotating health warning notices regarding the consequences of alcohol consumption.

Through the 1982 NIAAA public education campaign and outreach efforts conducted by the National Clearinghouse for Alcohol Information (NCALI), major voluntary associations embarked on alcohol abuse prevention for the first time. For example, the YWCA, with assistance from NCALI, developed a curriculum and provided technical assistance for the potential implementation of a prevention program in 900 local chapters. Many voluntary organizations included comprehensive prevention programs and activities on their agendas at the community level, thus increasing visibility for alcohol-related problems and prevention programing at the local level. Many businesses also joined this effort at the State and local levels.

In addition, in 1982, parent groups began to seek ways to prevent illegal and harmful alcohol use and misuse by youth. The previous focus of these groups was on the prevention of drug use; more recently, this attention has focused on alcohol and alcohol in combination with other drugs.

In the area of drinking and driving, other adult and youth community groups proliferated to prevent alcohol-related motor vehicle accidents. These various groups work to create a climate in which the community as a whole can be actively concerned about certain alcohol-related problems.

Probably one of the largest private sector initiatives to prevent alcohol and other drug problems among youth has been "The Chemical People," a two-part television broadcast aired in November 1983 in conjunction with the participation of more than 25 national organizations and 200 local public broadcast stations (PBS) across the country. Each participating PBS station and community volunteers organized town meetings to watch the programs and discuss community solutions unique to the problems of particular communities. The project was produced and pilot-tested by WQED in Pittsburgh with funding by the Richard King Mellon Foundation and the Metropolitan Life Foundation (WQED 1983).

The private sector is becoming increasingly involved in national, State, and local prevention activities. Insurance companies, the motor vehicle industry, soft drink producers and distributors, tire manufacturers, sports teams, privately owned print and broadcast outlets, producers and distributors of alcoholic beverages, and a wide range of other private sector businesses have contributed to prevention efforts.

The message communicated by these efforts indicates that there is and must continue to be a shared responsibility for prevention among different groups at all levels. This environment of concern has the potential for generating additional enthusiasm, commitment, and resolve to address alcohol problems.

Summary

The intent of this chapter has been to describe current perspectives on prevention, to summarize available research, and to describe current prevention efforts and initiatives. While national, State, and local prevention activities--often stimulated by grassroots movements--may be implemented without a scientifically based and sound methodological design, description of these efforts does suggest ideas for future prevention research.

Clearly, advances have been made in prevention since the Fourth Special Report (USDHHS 1981) was published. Previous research efforts focused on measuring the impact of single variables to determine changes in behavior and often failed to demonstrate significant differences. A broader range of prevention approaches is now being tested, however, and evaluations are being designed to test models in which myriad factors and variables interact in contributing to alcohol-related problems.

Although definitive answers may not be forthcoming in the immediate future, research findings suggest that both educational approaches and laws and regulations contribute to a reduction of alcohol problems. For these

to be effective, however, public support must be generated and sustained.

Given the complexity and interaction of factors affecting drinking patterns, occurrences, and consequences, no singular prevention strategy is likely to be optimal or universally generalizable. What is becoming eminently clear from previous and recent research is that a combination of diverse strategies must be employed. In this regard, a report entitled Beyond the Shadow of Prohibition published by the National Academy of Sciences in 1981 states that researchers:

> are convinced that the regulation of supply, legal and educational approaches to drinking practices, and interventions in the environment mediating between drinking and certain of its consequences represent valid approaches with promise for sustained improvement. Each detailed element will fail or succeed only as it is implemented properly and thoroughly; tactics that are undertaken as part of a broad and coordinated approach are more likely to be effective than ones undertaken in isolation. (Moore and Gerstein 1981, p. 116)

It is hoped that these combined approaches will be effective in reaching the alcohol-related health objectives of the Nation.

References

Alcocer, A.M. Alcohol use and abuse among the Hispanic American population. In: National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM)82-1193. Washington, D.C.: Supt of Docs., U.S. Govt. Print Off., 1982. pp. 361-384.

Alcohol, Drug Abuse, and Mental Health Administration. ADAMHA Prevention Policy and Programs 1979-1982. DHHS Pub. No. (ADM)81-1038. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981. 67 pp.

Armyr, G.; Elmer, A.; and Herz, U. Alcohol in the World of the 80's: Habits, Attitudes, Preventive Policies and Voluntary Efforts. Stockholm: Sober Förlags AB, 1982. 223 pp.

Bandura, A. Principles in Behavior Modification. New York: Holt, Rinehart & Winston, 1969.

Bandura, A. Social Learning Theory. Englewood Cliffs, N.J.: Prentice Hall, 1977.

Bandura, A. The self system in reciprocal determinism. American Psychologist 33(4):344-358, 1978.

Bandura, A. Self-Efficacy: An Integrative Construct. Stanford, Calif.: Stanford University, 1979.

Bartlett, E.E. Contribution of school health education to community health promotion: What can we reasonably expect? American Journal of Public Health 71(12):1384-1391, 1981.

Blane, H.T. Education and the prevention of alcoholism. In: Kissin, B., and Begleiter, H., eds. Social Aspects of Alcoholism. The Biology of Alcoholism, Vol. 4. New York: Plenum Press, 1976. pp. 519-578.

Blane, H.T., and Hewitt, L.E. Alcohol and Youth: An Analysis of the Literature 1960-75. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, March 1977. NTIS No. PB268698/AS.

Borkenstein, R.F. Problems of enforcement. In: Goldberg, L. ed. Alcohol, Drugs and Traffic Safety. Stockholm: Almquist and Wiskell International, 1981. pp. 818-837.

Boswell, B.N. The Cottage Program International, Inc. A Substance Abuse Prevention Program for the State of Utah. Final Report Analysis for Fiscal Year Ended June 30, 1983. Salt Lake City: The Cottage Program International, July 1983. 15 pp.

Botvin, G.J., and Eng, A. The efficacy of a multicomponent approach to the prevention of cigarette smoking. Preventive Medicine 11(2):199-211, 1982.

Braucht, G.N. Problem drinking among adolescents: A review and analysis of psychosocial research. In: National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM) 82-1193. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 143-164.

Brody, J.A. Aging and alcohol abuse. Journal of the American Geriatrics Society 30(2):123-126, 1982.

Bryan, W.A. Administering a campus alcohol program. In: Dean, J.C., and Bryan, W.A., eds. Alcohol Programming for Higher Education. Carbondale, Ill.: ACPA Media, 1982. pp. 44-57.

Colon, L. "Alcohol Control, Policies and Their Relation to Alcohol Consumption and Alcoholism." Ph.D. dissertation, Brandeis University, The F. Hellen Graduate School, 1980.

Cook, P. Effect of liquor taxes on drinking, cirrhosis, and auto accidents. In: Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. pp. 255-285.

Cook, P., and Tauchen, G. The effect of liquor taxes on heavy drinking. Bell Journal of Economics, 13(2):379-390, 1982.

Crisp, A.D. Making substance abuse prevention relevant to low-income black neighborhoods. II. Research findings. Journal of Psychedelic Drugs 12:139-156, 1980.

Dean, J.C. Alcohol programming: A conceptual model. In: Dean, J.C., and Bryan, W.A., eds. Alcohol Programming for Higher Education. Carbondale, Ill.: ACPA Media, 1982. pp. 15-29.

Donovan, B. "Collegiate Group for the Sons and Daughters of Alcoholics." Paper presented at NADC Conference, Washington, 1980. 17 pp.

Douglass, R.L.; Filkins, L.D.; and Clark, F.A. The Effect of Lower Legal Drinking Ages on Youth Crash Involvement. Final Report. Report No. UM-HSRI-AI-74-1-2. Washington, D.C.: National Highway Traffic Safety Administration, June 1974. NTIS No. PB 235-917.

Evans, G.B.; Steer, R.A.; and Fine, E.W. Alcohol value clarification in sixth graders: A film-making project. Journal of Alcohol and Drug Education 24(2):1-10, 1979.

Food and Drug Administration. Surgeon General's Advisory on Alcohol and Pregnancy. FDA Drug Bulletin 11(2):9-10, 1981.

Fullerton, M. A program in alcohol education designed for rural youth. Journal of Alcohol and Drug Education 24(2):58-62, 1979.

Gaines, J.J. Alcohol and the black woman. In: Harper, F.D., ed. Alcohol Abuse and Black America. Alexandria, Va.: Douglass Publishers, 1976. pp. 153-162.

Garza, R. El alcoholico [the alcoholic]. Impact 9(3):4-5, 1979.

Gibbs, J.P. Crime, Punishment, and Deterrence. New York: Elsevier, 1975. 272 pp.

Gomberg, E.S. Alcohol use and alcohol problems among the elderly. In: National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM)82-1193. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 263-290.

Goodstadt, M.S. Alcohol and drug education: Models and outcomes. Health Education Monographs 6(3):263-279, 1978.

Goodstadt, M.S., and Sheppard, M.A. Three approaches to alcohol education. Journal of Studies on Alcohol 44(2):362-380, 1983.

Goodstadt, M.S.; Sheppard, M.A.; and Chan, G.C. An evaluation of two school-based alcohol education programs. Journal of Studies on Alcohol 43:(3) 352-369, 1982.

Hames, L.N., and Petrucelli, E. Plan for influencing teenage drinking drivers. American Association for Automotive Medicine, October 1980. pp. 17-21.

Henggeler, S.W.; Sallis, J.F.; and Cooper, P.F. Comparison of university mental health needs priorities identified by professionals and students. Journal of Counseling Psychology 27(2): 217-219, 1980.

Hewitt, L.E. Current status of alcohol education programs for youth. In: National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM)82-1193. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 227-260.

Hingson, R.W.; Scotch, N.; Mangione, T.; Meyers, A.; Glantz, L.; Heeren, T.; Lin, N.; Mucatel, M.; and Pierce, G. Impact of legislation raising the legal drinking age in Massachusetts from 18 to 20. American Journal of Public Health 73(2): 163-170, 1983.

Hochheimer, J.L. Reducing alcohol abuse: A critical review of educational strategies. In: Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. pp. 286-335.

Holder, H.D., and Blose, J.O. Reduction of Community Alcohol Problems: A Computer Simulation for Wake County, North Carolina, Washington County, Vermont, and Alameda County, California. Chapel Hill, N.C.: The Human Ecology Institute, 1983. 229 pp.

Hundleby, J.D.; Carpenter, R.A.; Ross, R.A.J.; and Mercer, G.W. Adolescent drug use and other behaviors. Journal of Child Psychology and Psychiatry 23:(1)61-68, 1982.

Institute of Medicine. Legislative Approaches to Prevention of Alcohol-Related Problems: An Inter-American Workshop. Pub. No. IOM-82-003. Washington, D.C.: National Academy Press, 1982. 285 pp.

Irwin, K.C. "Women, Alcohol, and Drugs: A Feminist Course Focusing on Causes and Prevention of Abuse." Paper presented at the 104th Annual Meeting of the American Public Health Association, Miami, 1976.

Jessor, R., and Jessor, S. Problem Behavior and Psychosocial Development. New York: Academic Press, 1977. 281 pp.

Johnson, C.A.; Graham, J.W.; and Hansen, W.B. "Drug Use by Peer Leaders." Paper presented at the American Psychological Association annual meeting, Los Angeles, 1981.

Kola, L.A., and Kosberg, J.I. Model to assess community services for the elderly alcoholic. Public Health Reports 96(5):458-463, 1981.

Koski, H. Arbetsmarknaden och alkoholpriserna [Labor market and alcohol prices]. Alkoholpolitik 40:37-38, 1977.

Kraft, D.P. "A Program to Prevent Alcohol Problems Among College Students: Successes and Failures." Paper presented at the American Psychological Association annual meeting, Washington, D.C., 1982.

Leavy, R.L. First steps in campus prevention programs. CAFC News (Arlington, Va.), July-August 1980.

Leigh, D.H. "Prevention Work Among the Elderly: A Workable Model." Paper presented at the National Alcoholism Forum, Seattle, 1980.

Lillis, R.P.; Williams, T.P.; Chupka, J.Q.; and Williford, W.R. Highway Safety Considerations in Raising the Minimum Legal Age for Purchase of Alcoholic Beverages to Nineteen in New York State. Albany: New York State Division of Alcoholism and Alcohol Abuse, 1982. 15 pp.

Little, R.E. Change in obstetrician advice following a 2-year community education program on alcohol. Journal of Obstetrics and Gynecology, in press.

Little, R.E.; Streissguth, A.P.; and Guzinski, G.M. Prevention of fetal alcohol syndrome: A model program. Alcoholism: Clinical and Experimental Research 4(2):185-189, 1980.

Lucy, P. Can alcohol taxes reduce consumption?

Australian Journal of Alcoholism and Drug Dependence 6(4):119-122, 1979.

Maccoby, N., and Farquhar, J.W. Communication for health: Unselling heart disease. Journal of Communications 25:114-126, 1975.

Makela, K. Consumption level and cultural drinking patterns as determinants of alcohol problems. Journal of Drug Issues 5(4):344-357, 1975.

Makela, K. Differential effects of restricting the supply of alcohol: Studies of a strike in Finnish liquor stores. Journal of Drug Issues 10(1):131-144, 1980.

Makela, K.; Room, R.; Single, E.; Sulkunen, P.; and Wash, B. Alcohol, Society, and the State: A Comparative Study of Alcohol Control, Vol. I. Toronto: Addiction Research Foundation, 1981. 146 pp.

Malec, J. Metody zmniejszenia spozycia alkoholu [Methods of reducing alcohol consumption]. Problemy Alkoholizmu 27(4):3-4, 13, 1980.

Malin, H.; Coakley, J.; Kaelber, C.; Munch, N.; and Holland, W. An epidemiologic perspective on alcohol abuse in the United States. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM)82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 99-153.

Maxwell, D. Impact Analysis of the Raised Legal Drinking Age in Illinois. Washington, D.C.: National Highway Traffic Safety Administration, December 1981. 23 pp.

McAlister, A.L.; Perry, C.; and Maccoby, N. Adolescent smoking: Onset and prevention. Pediatrics 63(4):650-658, 1979.

McCartney, D.M., and Humbert, P. Evaluating the Prevention Demonstration: A Handbook for Grant Applicants. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, March 1978.

McCarty, D.; Poore, M.; Mills, K.C.; and Morrison, S. Direct mail techniques and the prevention of alcohol-related problems among college students. Journal of Studies on Alcohol 44(1):162-170, 1983.

McGuire, W.J. The nature of attitudes and attitude change. In: Lindzey, G., and Aronson, E., eds. Handbook of Social Psychology. Reading, Mass.: Addison-Wesley, 1969.

McIntyre, C.E. "Evaluating Prevention and Education: Fetal Alcohol Syndrome." Paper presented at the National Council on Alcoholism annual meeting, Seattle, 1980.

Mello, N.K. Behavioral studies of alcoholism. In: Kissin, B., and Begleiter, H., eds. Physiology and Behavior. The Biology of Alcoholism, Vol. 2. New York: Plenum Press, 1972. pp. 219-291.

Mills, K.C.; McCarthy, D.; Ward, J.; Minuto, L.; and Patzynski, J. A residence hall tavern as a collegiate alcohol abuse prevention activity. Addictive Behaviors 8(2):105-108, 1983.

Miranda, V.L. "Black Alcohol Prevention Programming: Past, Present, Future." Paper presented at NIAAA skills development workshop, Agenda for Black Alcoholism Programs. Jackson, Miss., 1981.

Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. 463 pp.

Mosher, J.F., and Mottl, J.R. The role of nonalcohol agencies in Federal regulation of drinking behavior and consequences. In: Moore, M.H., and Gerstein, D.R., eds. Alcohol and Public Policy: Beyond the Shadow of Prohibition. Washington, D.C.: National Academy Press, 1981. pp. 388-458.

Nathan, P.E., and Lisman, S.A. Behavioral and motivational patterns of chronic alcoholics. In: Tarter, R.E., and Sugerman, A.A., eds. Alcoholism: Interdisciplinary Approaches to an Enduring Problem. Reading, Mass.: Addison-Wesley, 1976. pp. 479-522.

National Association of State Alcohol and Drug Abuse Directors. Alcohol and drug abuse among the elderly: Out of sight, out of mind? NASADAD Alcohol and Drug Abuse Report, August 1981. 8 pp.

National Association of State Alcohol and Drug Abuse Directors. Alcohol and Drug Abuse Report. Special Report. Washington, D.C.: NASADAD, May 1983.

National Council on Alcoholism. "Prevention Position Paper." Unpublished NCA working document, June 11, 1982.

National Highway Traffic Safety Administration. Fatal Accident Reporting System, 1981: An Overview of U.S. Traffic Fatal Accident and Fatality Data Collected in FARS for Year 1981. Pub. No. DOT HS-806-251. Washington, D.C.: NHTSA, January 1983.

National Institute on Alcohol Abuse and Alcoholism. CASPAR Alcohol Education Program, Demonstration Curriculum Project. Final Report, 1979. Rockville, Md.: NIAAA, 1979.

National Institute on Alcohol Abuse and Alcoholism. Here's Looking at You Alcohol Education Project. Final Report, 1981. Rockville, Md.: NIAAA, 1981a.

National Institute on Alcohol Abuse and Alcoholism. Prevention of Alcohol Problems in Pre-Delinquent Youth. Final Report, 1981. Rockville, Md.: NIAAA, 1981b.

National Institute on Alcohol Abuse and Alcoholism. Report to the United States Congress on Federal Activities on Alcohol Abuse and Alcoholism, FY 1980. Rockville, Md..: NIAAA, 1982. 134 pp. and appendixes.

National Institute on Alcohol Abuse and Alcoholism. Implementing Public Health Education Campaigns: Lessons from Alcohol Abuse Prevention, An Evaluation of the National Institute on Alcohol Abuse and Alcoholism 1982 Alcohol Abuse Prevention Campaign. Rockville, Md.: NIAAA, January 1983. 37 pp. and appendixes.

Olegard, R.; Sabel, K.-G.; Aronsson, M.; Sandin, B.; Johansson, P.R.; Carlsson, C.; Kyllerman, M.; Iversen, K.; and Hrbek, A. Effects on the child of alcohol abuse during pregnancy: Retrospective and prospective studies. Acta Paediatrica Scandinavica (Supplement No. 275):112-121, 1979.

Perry, C.L., and Murray, D.M. "Peer Teaching in Smoking Prevention Research: Theoretical Considerations in Intervention Strategies." Paper presented at the American Psychological Association annual meeting, Los Angeles, 1981.

Portnoy, B. Effects of a controlled-usage alcohol education program based on the Health Belief Model. Journal of Drug Education 10(3):181-195, 1980.

Pringle, H.; Gregory, J.; Ginkel, K.; and Cheek, C. Alpha Centers: A viable prevention model for substance abuse agencies and public schools. In: Schecter, A.J., ed. Social and Behavioral Issues. Drug Dependence and Alcoholism, Vol. 2. New York: Plenum Press, 1981. pp. 183-189.

Resource Alternatives Corporation. Prevention of Alcohol Abuse Among Pre-Delinquent Youth: An Overview of the Evaluation Results. Washington, D.C.: RAC, 1982.

Roizen, J. Estimating alcohol involvement in serious events. In: National Institute on Alcohol Abuse and Alcoholism. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1. DHHS Pub. No. (ADM)82-1190. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 179-219.

Rosett, H.L.; Weiner, L.; Zuckerman, B.; McKinlay, S.; and Edelin, K.C. Reduction of alcohol consumption during pregnancy with benefits to the newborn. Alcoholism: Clinical and Experimental Research 4(2):178-184, 1980.

Rosett, H.L.; Weiner, L.; Lee, A.; Zuckerman, B.; Dooling, E.; and Oppenheimer, E. Patterns of alcohol consumption and fetal development. Obstetrics and Gynecology 61(5):539-546, 1983.

Ross, H.L. Deterrence of the Drinking Driver: An International Survey. Washington, D.C.: National Highway Traffic Safety Administration, 1981. 121 pp.

Rotter, J.B. Generalized expectancies in internal versus external control of reinforcement. In: Rotter, J.B.; Chance, J.E.; and Phares, E.J., eds. Application of Social Learning Theory of Personalities. New York: Holt, Rinehart & Winston, 1972.

Sandmaier, M. "Women and Alcohol Abuse: A Strategy for Defense." Paper presented at the 104th Annual Meeting of the American Public Health Association, Miami, 1976.

Schaefer, J.M. Ethnic and racial variations in alcohol use and abuse. In: National Institute on Alcohol Abuse and Alcoholism. Special Population Issues. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM)82-1193. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 293-311.

Smart, R.G. The impact of prevention measures: An examination of research findings. In: Institute of Medicine. Legislative Approaches to Prevention of Alcohol-Related Problems: An Inter-American Workshop. Pub. No. IOM-82-003. Washington, D.C.: National Academy Press, 1982. pp. 224-246.

Smith, R. Relation between consumption and damage. British Medical Journal 283(6296):895-898, 1981.

Somervuori, A. Prisskruven som alkoholpolitriskt medel [Pricing as an alcohol policy]. Alkoholpolitik 40:85-93, 1977.

Staulcup, H.; Kenward, K.; and Frigo, D. A review of Federal primary alcoholism prevention projects. Journal of Studies on Alcohol 40(11): 943-968, 1979.

Streissguth, A.P.; Darby, B.L.; Barr, H.M.; Smith, J.R.; and Martin, D.C. Comparison of drinking and smoking patterns during pregnancy over a six-year period. American Journal of Obstetrics and Gynecology 145(6):716-724, 1983.

Stuart, R.B. Teaching facts about drugs: Pushing or preventing? In: Ward, D.A., ed. Alcoholism: Introduction to Theory and Treatment. Dubuque, Iowa: Kendall/Hunt, 1980. pp. 211-225.

Sulkunen, P. Developments in the Availability of Alcoholic Beverages in the EEC Countries. Helsinki: Social Research Institute of Alcohol Studies, 1978. 93 pp.

Tofany, V.L. The council's plan of action. Traffic Safety, March/April 1983.

U.S. Department of Health and Human Services. Fourth Special Report to the U.S. Congress on Alcohol and Health. De Luca, J. R., ed. DHHS Pub. No. (ADM)81-1080. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1981.

U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. Prevention '82. DHHS (PHS) Pub. No. 82-50157. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. 168 pp.

WQED Television. What Does It Take To Fight School-Age Drug and Alcohol Abuse? Pamphlet in The Chemical People series. Pittsburgh, Pa.: WQED, 1983.

Wagenaar, A.C. "The Minimum Legal Drinking Age: A Times-Series Impact Evaluation." Ph.D. dissertation, University of Michigan, 1980.

Wagenaar, A.C.; Douglass, R.L.; and Compton, C.P. Raising the Legal Drinking Age in Michigan and Maine. Report No. UM-HSRI-81-58. Rockville, Md.: National Institute on Alcohol Abuse and Alcoholism, 1981. 367 pp.

Wallack, L.M. Mass media campaigns: The odds against finding behavior change. Health Education Quarterly 8(3):209-260, 1981.

Weisheit, R. A.; Kearney, K.A.; Hopkins, R.H.; and Mauss, A.L. Evaluation of a Model Alcohol Education Project for the Public Schools: Phase II. An Overview of the First Year's Activities and Results. Pullman: Washington State University, 1979.

Williams, A.F.; Zador, P.L.; Harris, S.S.; and Karpf, R.S. The effect of raising the legal minimum drinking age on fatal crash involvement. Journal of Legal Studies 12:169-179, 1983.

Wittman, F.D. Current status of research demonstration programs in the primary prevention of alcohol problems. In: National Institute on Al-

cohol Abuse and Alcoholism. Prevention, Intervention, and Treatment: Concerns and Models. Alcohol and Health Monograph No. 3. DHHS Pub. No. (ADM)82-1192. Washington, D.C.: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp.3-57.

World Health Organization. Alcohol control policies. In: Robinson, D., ed. Alcohol Problems. New York: Holmes and Meier, 1979. pp. 227-231.

World Health Organization. Problems Related to Alcohol Consumption. Report of a WHO Expert Committee. Technical Report Series 650. Geneva, Switzerland: WHO, 1980. 72 pp.

Index

Abstinence
  and cognitive deficits, 27, 28
  with disulfiram treatment, 112-113
  and healthy offspring, 69, 76, 130
  vs. moderate drinking, 111
  and psychiatric symptoms, 29
  as treatment outcome, 105, 113, 115
Accidents, alcohol-related
  airplane, 85
  home and recreational, 86-87
  pedestrian, xix, 85
  traffic (see also Driving and drinking), xix, 9-11, 83-84
  work-related, xix, 85-86
Adolescents
  alcohol education programs for, xxii, 125-126
  consumption patterns in, xiii, 3-5
  Initiative on Teenage Alcohol Abuse, 134
  in single-vehicle fatal accidents, 9-11, 83
  tobacco education programs for, 127-128
Age (see also Drinking age, minimum)
  and AA membership, 112
  and alcohol education programs, 123, 125-127
  re alcohol and homicide, 87-88
  and brain scan measurements, 27
  and early detection of alcoholism, 104-105
  as factor in consumption, 2-3, 4
  in fatal traffic accidents, 9-11, 83
  interaction with alcohol consumption, 26
  re suicide, 92-93
Alcohol abuse (see also Alcoholism)
  based on reinforcement theory, 37-38
  costs of, v, 93-95, 96
  definitions regarding, xiii, 101
  historical perspective on, x
  and psychiatric illnesses, 29, 114
Alcohol dependence (see also Alcoholism)
  defined as syndrome, 101-103
  early detection of, 104-105
  related to tolerance, 36-37, 101, 102
Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA)
  prevention definitions, 123
  role in ICD development, xx, 101
Alcohol metabolism
  genetic variation, 20, 21
  inability in heart, 52
  in Orientals ("flushing"), 20, 21
  role of liver in, 48-50
  and sexual dysfunction, 55
  TIQ formation and uncontrolled drinking, xvi, 38
Alcoholic Rehabilitation Act, enactment of, x
Alcoholics Anonymous (AA), xi, xxii, 111-112, 114
Alcoholism (see also Alcohol abuse; Alcohol dependence)
  as cause of death, 6-7
  cognitive effects of, 27
  and depression, 29
  diagnosis of, xiii, 101-103
  and family problems, 89
  hospital discharges with, 8, 9
  and rape, 89
  subtypes, heritability of, 18-19
  theories
    denial of responsibility, 91
    disinhibition, 87, 89, 91
    interactive drinking/violence, 91
    social learning, 89, 91
  and traffic accidents, 84
Alcoholism counselors, xi, 113
Alzheimer's disease
  compared with alcoholic brain injury, xv, 28
Animal studies
  on alcohol and cancer, 59
  on alcohol and digestive system, 45, 46, 47-48
  on alcoholic blood disorders, 53-54
  on alcohol metabolism, 48
  on alcohol-related birth effects, 71-72, 73, 74, 75, 77
  on alcohol withdrawal, 35
  on calcium uptake and binding, 34
  on cognitive skills, 26, 28
  on electrical activity in neurons, 33
  on genetic susceptibility to alcoholism, 21
  on heart effects of alcohol, 52
  on hormonal changes, 56, 57-58
  on reinforcement theory, 37-38
  on sexual dysfunction, 55-56
  on tolerance, 21, 35, 36
Antabuse (see Disulfiram)

Beverage type
  in birth effects, 77
  in consumption per capita, 1
Biochemical markers for alcoholism
  in early diagnosis, xii, xxi, 104-105
  elevated AANB (alpha amino N-butyric acid) in blood, 49
  elevated GGTP (serum gamma-glutamyl transpeptidase), xxi, 104
  elevated MCV (mean corpuscular volume), xvii, 54, 104
Birth effects, alcohol-related (see also Fetal alcohol syndrome)
  in animal studies, 71-72, 73, 74, 75, 77
  low birth weight, xviii, 69, 73-74, 76
  fetal alcohol syndrome, xviii, 70-71

Birth effects, alcohol-related (cont.)
hyperactivity, xviii, 69, 74
infant mortality, 69
mental retardation, xviii, 74
motor development scores, xviii, 74
neural development, 75
problems with human studies, 71
spontaneous abortion, xviii, 69, 72
Black Americans
males and suicide, 92
pregnancy and drinking, 6
prevention programs for, 129
Blood
abnormalities with liver disease, 49
disorders from alcohol
elevated MCV (mean corpuscular volume), 54
altered clotting factors, 54
leukopenia, 54
megaloblastic anemia, 53
vitamin deficiencies, 53
effects of heavy alcohol use on, xvii
Blood alcohol concentration (BAC)
legal standard for intoxication, xix
levels in fatal accidents, 9-11, 83-86
level of impairment, 25
Brain (see also CAT scans; Cognition; EEG recordings)
damage in alcohol-affected fetuses, 74
effects of alcohol on, xv-xvi
measurement for alcohol dependence, 27

Caffeine
as antidote to alcohol, 26
Cancers and alcohol
of digestive tract, xvi, 45, 46, 59
of liver, 59
of pancreas, xvii, 48, 59
CAT (computer-assisted tomography) scans
in measuring brain for alcoholism, xv, 27
Children
alcohol education programs for, 123, 125
of alcoholics, 91-92
conduct disorders as alcoholism predictors, 17
Cirrhosis, alcoholic
blood abnormalities in, 49
as cause of death, xvii, 6-7
description of pathology, 50-51
hormonal changes in, 57, 58
hospital discharges with, 8, 9
Cognition, effects of alcohol on
in alcoholics, 27
driving-related skills, xv, 25, 84
role in treatment models, 110
in social drinkers, 26
and violent crime, 87, 88
Consumption of alcohol
measured by sales, 1-2
per capita, by State, xiii, 1-2, 3
per capita, by type, 1-2
in pregnancy, 75-76
self-reported, 2-6, 77
surveys, 2-6

Costs of alcohol abuse
economic
of birth defects, 71
illness-specific estimates, 94, 95, 96
population-specific estimates, 94
in work productivity, 93-94
effect of treatment on, 106-107
under Blue Cross/Blue Shield, 107
within health maintenance organizations (HMOs), 107
social, 94
Counselors, alcoholism, xi, 113
Crime, role of alcohol in
homicide, xix, 87-88, 90
other, 89, 90
rape, xix-xx, 88-89, 90

Dementia, alcoholic
chronic organic brain syndrome, 28-29
DSM-III evaluation, 101
Dependence (see Alcohol dependence)
Depression
and alcohol use, xx, 29, 30
and suicide, 92
Detoxification
in nonhospital ("social") settings, xxi, 106
and regaining cognitive skills, 27
Diagnosis of alcoholism
biochemical markers, xii, xxi, 104
difficulty in, 84, 100, 115
DSM-III, role of, xx, 101-103
ICD, role of, xx, 101
psychosocial indicators
Michigan Alcoholism Screening Test (MAST), 104
Munich Alcoholism Test, xxi, 104
unitary disease concept, 100, 114
binary classification rule, 100
continuum of severity, 100-101
Diet
and alcoholic brain injury, xv
and blood disorders, 46, 53
contribution to alcoholism, 27-28
and liver damage, xvii, 48, 49
and pregnancy outcome, 72
and vitamin deficiencies, xvi, 46
Digestive tract
cancers of, xvi, 45, 46, 48, 59
effects of alcohol on, xvi
esophagus, 45
intestine, 46-47
mouth, 45
pancreas, 47-48
stomach, 45-46
Disulfiram (Antabuse)
effectiveness as treatment, xxii, 112-113
Diuresis, alcoholic, 58
Drinking age, minimum
effectiveness in prevention, xxii, 132-133
Driving and drinking (see also under Cognition; Driving while intoxicated arrests)
and fatal accidents, 83-85
legal prevention, 133
public reaction to, xi, 84-85, 122

Driving while intoxicated (DWI) arrests
drivers in fatal accidents, 11, 84
prevention programs, 135
and violent crime, 88
DSM-III (Diagnostic and Statistical Manual of Mental Disorders)
definitions, alcohol-related, 101
differential assessment, 103
evaluation axes, 101
interview schedules, 101
uniform standards for diagnosis, xx, 102

Education programs
and drinking during pregnancy, 76, 78
effectiveness in prevention, xxii, 123, 125-127
school-based
for adolescents, 125-126, 127-128
for elementary-age children, 123, 125
for young adults, 126-127
work-related wellness programs, 128
EEG (electroencephalogram) recordings
average evoked response (AER), 31
and brain model of intoxication, 30
Elderly
prevention programs for, 129-130
treatment needs of, 108
vulnerability to alcohol, 26
Employee assistance programs
effect on productivity, 93-94
role in treatment, xi, xxi, 105
wellness programs, 128
Endocrine system (see Hormones)
Environment
in family alcoholism, 15-19
in physiological responses, 19-20

Family life, alcohol-affected
children of alcoholics, 91-92
separation and divorce, 89
violence
child abuse, 90, 91
spouse abuse, 90-91
Fatty liver, alcoholic
description of pathology, 50-51
Fetal alcohol syndrome (FAS)
characteristics of, xviii, 70
economic impact of, 71
genetic factors and, 71
prevalence of, 70-71
prevention programs on, 130

Genetic factors
in alcoholic cirrhosis, 51
in alcoholic subtypes, 114
in birth effects, 71, 77-78
in chronic pancreatitis, 48
vs. environment in family alcoholism, 15-19
among minority populations, 129
in physiological responses to alcohol, 19-21

Health insurance
role in treatment, xi, xxi, 106-107
Heart
effects of alcohol on, xvii
cardiac arrhythmias, 52
Heart (cont.)
cardiomyopathy, alcoholic, 51
moderate alcohol use, benefits of, 51-52
Hepatitis, alcoholic
blood abnormalities in, 49
description of pathology, 50-51
Heredity (see also Genetic factors; Pregnancy outcome)
role in predicting for alcoholism, xii, xiii-xv
Hispanic Americans
pregnancy and drinking, 6
rates of alcoholism, 129
treatment programs for, 108-109
Hormones
action in alcohol metabolism, 48
altered by alcoholism, xvii-xviii
glucagon, 58
growth hormone, 57
hypothalamus-pituitary-adrenal axis, 56-57
insulin, 58
oxytocin, 58
parathormone, 58
prolactin, 57-58
sexual dysfunction, 55-56
thyroid, 57
vasopressin, 58
Hospitalization
alcohol-related causes of, 7-8
and cost-benefit analysis, 107
for detoxification, 106
and treatment effectiveness, 107-108
Hypocalcemia, alcoholic, 58
Hypoglycemia, alcoholic, 58-59
in fetal growth retardation, 73
and violent crime, 87

Immune response
diminished in alcoholics, xvii
role in alcoholic liver damage, 54
ICD (International Classification of Diseases)
role in diagnosis, xx
updating, 101
Insurance (see Health insurance)
Intervention (see Prevention; Treatment)

Kidney
disease in alcoholics, 54

Liver
effects of alcohol on, xvii, 48-51
disease and behavioral deficits, 30
disease and glucose tolerance, 58
disease and sexual dysfunction, 55, 56
Lung
disease in alcoholics, 54-55

Mass media campaigns
effectiveness in prevention, xxii-xxiii, 127
for women and youth, 135
Metabolism (see Alcohol metabolism)
Minority and special populations (see Adolescents; Black Americans; Children; Elderly; Hispanic Americans; Native Americans; Orientals; Women; Young adults)

Moderate drinking
and birth effects, 77
and relapse rate in alcoholics, 105, 110-111
and social problems, 83
Muscle, skeletal
myopathy, alcoholic, 52-53
Muscle, smooth
in esophagus, alcohol and, 53
in uterus, alcohol and, 53

National Academy of Sciences
legislative approaches to prevention, 131
prevention policy, 123, 134
National Center for Health Statistics
Hospital Discharge Survey, 7-8
pregnancy and drinking behavior surveys, 5-6
National Council on Alcoholism, 136
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
establishment of, x
fatal accident studies, 83
national drinking pattern surveys, 2-3
pregnancy outcome and alcohol studies, 71
prevention efforts, 127, 133-134
National Institute on Drug Abuse (NIDA)
alcohol consumption surveys, 3-5
Native Americans
alcohol-related hospitalizations, 8-9
alcohol-related mortality among, 8
treatment programs for, 108-109
Neurons (nerve cells)
in alcohol effects, 31
in alcohol-related birth effects, 75, 77
chemical transmission between, 34-35
description and function, 31-33
electrical conduction in, 33-34
neuronal membrane, xvi, 35-37
Nutrition (see Diet)

Orientals, genetic studies, 20, 21
Objectives for the Nation (in 1990), xii, 124

Pancreatitis, chronic
in alcoholics, xvi, 47-48
and glucose tolerance, 58
Pregnancy outcome (see also Birth effects, alcohol-related)
consumption patterns and, xi, xviii, 5-6, 75-76, 77
historical risks to, 69-70
and paternal drinking, xviii, 76
and prevention efforts, 78, 130
Prevention of alcohol-related problems
and birth effects, 78
current activities
"The Chemical People," 136
National Council on Alcoholism, 136
State and local efforts, 134-136
U.S. Government agencies, 133-134
volunteer organizations, 136
World Health Organization, 133
education programs, xxii, 78, 123, 125-127, 128
drinking age, minimum, xxii, 132-133

Prevention of alcohol-related problems (cont.)
grassroots involvement, 122, 134
law enforcement policy, xxii, 84-85, 130-131, 133
mass media campaigns, xxii-xxiii, 127
National Academy of Sciences study on, 123
primary (with children), xi
public health approach to, 123
research findings on, 122
secondary (early intervention), 100, 104-105, 130
for special populations, 128-130
through taxation, xxiii, 131-132
Psychiatric illnesses
and alcohol abuse, 29, 114
Psychosis, alcoholic (Korsakoff's)
as cause of death, 6-7
chronic organic brain syndrome, xv, 28-29
hospital discharges with, 8, 9

Sex (see also Women)
as factor in consumption, 2, 4
as factor in hospital discharges with alcoholism, 8
Sexuality
altered by alcoholism, 55-56
effects of alcohol on, xvii-xviii
Suicide
role of alcohol in, xx, 29, 92-93

Taxation
as prevention approach, xxiii, 131-132
Teenagers (see Adolescents; Young adults)
Teratology (see Birth effects, alcohol-related; Fetal alcohol syndrome)
Therapy (see Treatment)
Thiamine (vitamin B_1)
deficiency in alcoholics, xv, 27-28, 46-47
and heart disease, 51
and Wernicke's encephalopathy, 28-29
and Wernicke-Korsakoff syndrome, 20
Time of day/week
as factor in traffic accidents, 11, 12, 84
Tobacco
combined effect with alcohol, xv, xvi, 26
in digestive tract, 45, 59
in fatal fires, 86-87
in fatal traffic accidents, 84
in fetal abnormalities, 74
in lung disease, 54
education programs for adolescents, 127-128
Tolerance
in alcohol dependence syndrome, 101, 102
and genetic influence, 21
and neurochemical changes in brain, 34
role of hormonal systems in, 36
role of learning in, 36
Treatment of alcohol-related problems
approaches
Alcoholics Anonymous, xxii, 111-112, 114
behavior therapy, xxii, 109-110
family therapy, xxii, 112, 114
job-related, 105
pharmacotherapy, xxii, 29, 35, 112-113
psychotherapy, xxii, 112
cost-benefit analysis of, 107

Treatment of alcohol-related problems (cont.)
detoxification, xxi, 106
diagnosis and, xx, 100-104, 114-115
and early intervention, xxi, 104
goals, 110-111
insurance coverage for, xi, xxi, 106-107
multiple substance abuse programs, 109
outcomes, 105, 112-116
recent developments in, xi, 100, 105, 114, 115-116
settings, 107-108
targeted to special populations, xxi-xxii, 108-109

Uniform Alcoholism and Intoxication Treatment Act
effect on treatment, 106

Veterans Administration (VA)
alcohol-related hospitalizations, 8
Victims, alcohol in, 88, 89
Violence (see Crime)
Vitamins and minerals (see also Thiamine)
in alcoholic hypocalcemia, 58
deficiencies in alcoholics, 45-48, 53
riboflavin as treatment, 112

Withdrawal, alcohol
in alcohol dependence syndrome, 101, 102
convulsions, 35
and detoxification, 106
hormonal effects of, 56-57, 58
and treatment with tricyclic antidepressants, 113
Women (see also Pregnancy outcome)
alcoholics and depression, 92
and AA membership, 112
consumption patterns, 75-76
prevention programs for, 128-129, 135
treatment needs of, 108
World Health Organization (WHO)
current activities, 133
dependence syndrome, xxi, 101-103
and international alcohol policy, 130-131
role in ICD development, xxi, 101

Young adults
alcohol education programs for, xxii, 126-127, 135
consumption patterns in, 2-5
in single-vehicle fatal accidents, 9-11
Youth (see Adolescents; Young adults)

☆ U.S. GOVERNMENT PRINTING OFFICE 1984 442-667/18416